

JAN 05 2007



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IPR

In re Applicant:

Oron YACOBY-ZEEVI et al

Serial No.: 10/645,659

Filed: August 22, 2003

Group Art Unit: 1644

For: Heparanase Activity Neutralizing Anti-Heparanase  
Monoclonal Antibody And Other Anti-Heparanase  
Antibodies

Attorney  
Docket: 26128

Examiner: DIBRINO, MARIANNE NMN

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

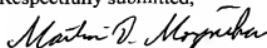
Sir:

Enclosed is a PTO Form 1449 which lists citations which may be material to the patentability and examination of the above identified application. Also enclosed are copies of the references cited. These are submitted in compliance with the duty of disclosure defined in 37 CFR 1.56. The Examiner is requested to make these citations of official record in this application.

This is a continuation in part of U.S. Patent Application No. 10/368,044, filed February 19, 2003, which also claims priority as a continuation from U.S. Patent Application No. 09/186,200, filed November 4, 1998, now U.S. Patent No. 6,562,950, issued May 13, 2003, which is a continuation-in-part of U.S. Patent Application No. 09/071,739, filed May 1, 1998, now U.S. Patent No. 6,177,545, issued January 23, 2001, which is a continuation-in-part of U.S. Patent Application No. 08/922,170, filed September 2, 1997, now U.S. Patent No. 5,968,822, issued October 19, 1999. This application also claims priority from U.S. Patent Application No. 10/456,573, filed June 9, 2003, which is a continuation-in-part of U.S. Patent Application No. 09/435,739, filed November 8, 1999, which is a continuation of U.S. Patent Application No. 09/258,892, filed March 1, 1999, now expired, which is a continuation-in-part of PCT Application No. PCT/US98/17954, filed August 31, 1998, now expired. All of these applications are hereby incorporated by reference as if fully set forth herein.

This Supplemental Information Disclosure Statement under 37 CFR 1.56 is not to be construed as a representation that a search has been made, that additional matter which is material to the examination of this application does not exist, or that any or more of these citations constitutes prior art.

Respectfully submitted,



Martin D. Moynihan  
Registration No. 40,338

Dated: December 31, 2006

03/13/2008



Sheet 1 of 3

Atty. Docket No. 910/12 Application No. 09/186,200

APPLICANT  
Tuvia PERETZ et al

Filing Date Group Art Unit

INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
AA						

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION	
						YES NO	
AB							

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AC	Wight et al, "The Role of Proteoglycans in Cell Adhesion, Migration and Proliferation", <i>Curr. Opin. Cell Biol.</i> , 4:793-801, 1992
AD	Jackson et al, "Glycosaminoglycans: Molecular Properties, Protein Interactions and Role in Physiological Processes", <i>Physiol. Rev.</i> , 71:481-539, 1991
AE	Wight et al, "Cell Biology Of Arterial Proteoglycans", <i>Arteriosclerosis</i> , 9:1-20, 1989
AF	Kjellen et al, "Proteoglycans: Structures and Interactions", <i>Annu. Rev. Biochem.</i> , 60: 443-475, 1991
AG	Ruosahti et al, "Proteoglycans as Modulators of Growth Factor Activities", <i>Cell</i> , 64: 867-869, 1991
AH	Vlodavsky et al, "Extracellular Matrix-Bound Growth Factors, Enzymes and Plasma Proteins" In <i>Basement Membranes: Cellular and Molecular Aspects</i> (eds. Rohrbach and Timpl), Academic Press, Inc., Orlando, Fla., 327-343, 1993
AI	Vlodavsky et al, "Expression of Heparanase by Platelets and Circulating Cells of the Immune System: Possible Involvement in Diapedesis and Extravasation", <i>Invasion &amp; Metastasis</i> , 12: 112-127, 1992
AJ	Vlodavsky et al, "Inhibition of Tumor Metastasis by Heparanase Inhibiting Species of Heparin", <i>Invasion &amp; Metastasis</i> , 14: 290-302, 1995
AK	Nakajima et al, "Heparanase and Tumor Metastasis", <i>J. Cell Biochem.</i> , 36: 157-167, 1988
AL	Liotta et al, "Tumor Invasion and the Extracellular Matrix", <i>Lab. Invest.</i> , 49: 639-649, 1983
AM	Vlodavsky et al, "Lymphoma Cell Mediated Degradation of Sulfated Proteoglycans in the Subendothelial Extracellular Matrix", <i>Cancer Res.</i> , 43: 2704-2711, 1983
AN	Vlodavsky et al, "Involvement of Heparanase in Tumor Metastasis and Angiogenesis", <i>Isr. J. Med.</i> , 24: 464-470, 1988

EXAMINER Marianne Dibrino/ DATE CONSIDERED 03/13/2008

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form FTO-1449 (Modified)

Atty. Docket No.  
910/12Application No.  
05/186,200INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)APPLICANT  
Tuvia PERETZ et al

Filing Date

Group Art Unit

## U.S. PATENT DOCUMENTS

	EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BA							

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CL/SS	TRANSLATION	YES	NO
BB								

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

BC	Parish et al, "Evidence that Sulfated Polysaccharides Inhibit Tumor Metastasis by Blocking Tumor Cell-Derived Heparanase", <i>Int. J. Cancer</i> , 40: 511-517, 1987
BD	Vlodavsky et al, "Morphological Appearance, Growth Behavior and Migratory Activity of Human Tumor Cells Maintained on Extracellular Matrix vs. Plastic", <i>Cell</i> , 19: 607-616, 1980
BE	Vlodavsky et al, "Extracellular Sequestration and Release of Fibroblast Growth Factor: A Regulatory Mechanism?", <i>Trends Biochem. Sci.</i> , 16: 268-271, 1991
BF	Campbell et al, "Heparin Sulfate-Degrading Enzymes Induce Modulation of Smooth Muscle Phenotype", <i>Exp. Cell Res.</i> , 200: 156-167, 1992
BG	Lider et al, "Suppression of Experimental Autoimmune Diseases and Prolongation of Allograft Survival by Treatment of Animals with Heparinoid Inhibitors of T Lymphocyte Heparanase", <i>J. Clin. Invest.</i> , 83: 752-756, 1989
BH	Thunberg et al, "The Molecular Size of the Antithrombin-Binding Sequence in Heparin", <i>FEBS Lett.</i> , 117: 203-206, 1980
BI	Goldberg et al, "An Improved Method for Determining Proteoglycans synthesized by Chondrocytes in Culture", <i>Connective Tissue Res.</i> , 24: 265-275, 1990
BJ	Hudson, PJ, "Recombinant Antibody Fragment", <i>Curr. Opin. Biotech.</i> , 4: 395-401, 1993
BK	Schoepf et al, "Neutralization of Hemolytic and Mouse Lethal Activities of <i>C. Perfringens</i> Alpha-Toxin Need Simultaneous Blockage of Two Epitopes by Monoclonal Antibodies", <i>Microbiol. Pathogenesis</i> , 23: 1-10, 1997
BL	Chiba et al, "Generation of Neutralizing Antibody to the Reverse Transcriptase of Human Immunodeficiency Virus Type 1 by Immunizing of Mice with an Infectious Vaccine Virus Recombinant", <i>J. Immunological Methods</i> , 207: 53-60, 1997
BM	Wong, JF, "Monoclonal Antibodies: Therapeutic Applications Grow in Promisc and Number", <i>Genetic Engineering News</i> , July, 1998, pp 23, 49

EXAMINER /Marianne Dibrino/

DATE CONSIDERED 03/13/2008

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 608; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

Atty. Docket No.  
910/12Application No.  
01/186,200INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)APPLICANT  
Tuvia PERETZ et al

Filing Date      Group Art Unit

## U.S. PATENT DOCUMENTS

	EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
CA							
CB							
CD							
CE							
CF							
CG							
CH							
CI							
CJ							

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
							YES
CH							NO

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CI	Sherman-Gold, R., "Monoclonal Antibodies: The Evolution from '80s Magic bullets to Mature, Mainstream Applications as Clinical Therapeutics", <i>Genetic Engineering News</i> , August, 1997, pp 4, 35
CJ	Danheiser, SL, "Rituximab Leads Line Of Hopeful Mab Therapies, yet FDA still has Bulk Manufacture Concerns", <i>Genetic Engineering News</i> , October, 1997, pp 1,6,33,38
CK	Rader et al, A Phage Display Approach for Rapid Antibody Humanization: Designed Combinatorial V Gene Libraries", <i>Proc. Natl. Acad. Sci.</i> , 95: 8910-8915, 1998
CL	Mateo et al, "Humanization of a Mouse Monoclonal Antibody that Blocks the Epidermal Growth Factor Receptor: Recovery Antagonistic Activity", <i>Immunotechnology</i> , 3: 71-81, 1997
CM	
CN	
CO	
CP	

EXAMINER	/Marianne Dibrino/	DATE CONSIDERED	03/13/2008
----------	--------------------	-----------------	------------

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

JAN 05 2007  
PATENT & TRADEMARK OFFICE

PTO/SB/08a (08-03)

Approved for use through 07/31/2006, OMB 0651-0031

U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 23

Complete if Known	
Application Number	10/645,659
Filing Date	August 22, 2003
First Named Inventor	Oron YACOBY-ZEEVI et al
Art Unit	1644
Examiner Name	DIBRINO, MARIANNE NMN

Attorney Docket Number 26128

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/MD/	1	US-5,997,863	07-7-1999	Zimmermann et al.	
	2	US-5,688,679	11-18-1997	Powell	
	3	US-6,387,643	05-14-2002	Heinrikson et al.	
	4	US-6,423,312	07-23-2002	Yacoby-Zeevi	
	5	US-6,531,129	03-11-2003	Pecker et al.	
	6	US-4,455,296	06-19-1984	Hansen et al.	
	7	US-5,571,506	05-5-1996	Regan et al.	
	8	US-5,917,830	06-29-1999	Chen et al.	
	9	US-5,859,660	01-12-1999	Perkins et al.	
	10	US-5,600,366	04-4-1997	Schulman	
	11	US-6,020,931	01-1-2000	Bilbrey et al.	
	12	US-6,153,187	11-28-2000	Yacoby-Zeevi	
	13	US-5,145,679	08-8-1992	Hinson	
	14	US-5,736,137	07-7-1998	Anderson et al.	
	15	US-5,194,596	03-16-1993	Tischer et al.	
	16	US-5,350,836	09-27-1994	Kopchick et al.	
	17	US-6,562,950	05-13-2003	Peretz et al.	
	18	US-5,580,862	03-3-1996	Rosen et al.	
	19	US-5,474,983	12-12-1995	Kuna et al.	
	20	US-2002/0102560	8 01-1-2002	Pecker et al.	
	21	US-5,618,709	08-8-1997	Gewirtz et al.	
	22	US-5,656,595	08-12-1997	Schweighoffer et al.	
	23	US-4,683,195	07-28-1987	Mullis et al.	
	24	US-5,602,095	02-11-1997	Pastan et al.	
	25	US-4,117,841	03-3-1978	Perrotta et al.	
	26	US-2003/0161823	08-28-2003	Ilan et al.	
	27	US-5,962,321	05-5-1999	Gough et al.	
	28	US-5,830,759	03-3-1998	Chang et al.	
	29	US-6,230,151	08-8-2001	Agrawal et al.	
	30	US-5,799,311	08-25-1998	Agrawal et al.	
	31	US-6,314,420	06-6-2001	Lang et al.	
	32	US-4,937,747	06-26-1990	Koller	
	33	US-6,307,965	10-23-2001	Aggarwal et al.	
	34	US-6,226,792	01-1-2001	Goiffon et al.	
	35	US-5,859,929	01-12-1999	Zhou et al.	
	36	US-5,799,276	08-25-1998	Komissarchik et al.	
/MD/	37	US-2002/0068061	06-6-2002	Peretz et al.	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.<sup>1</sup> Applicant's unique citation designation number (optional).<sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 801.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.<sup>5</sup> Kind of document by the two-letter code as indicated on the document under WIPO Standard ST. 16 if possible.<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14, this collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P. O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

03/13/2008

/Marianne Dibrino/

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet 2 of 23

*Complete if Known*

Application Number	10/645,659
Filing Date	August 22, 2003
First Named Inventor	Oron YACOBY-ZEEVI et al
Art Unit	1644
Examiner Name	DIBRINO, MARIANNE NMN

Attorney Docket Number 26128

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/MD/	38	US-5,360,735	01-1-1994	Weinshank et al.	
	39	US-2002/0088019	04-4-2002	Yacoby-Zeevi	
	40	US-5,589,604	12-31-1996	Drohan et al.	
	41	US-5,700,671	12-23-1997	Prieto et al.	
	42	US-5,714,345	03-3-1998	Clark	
	43	US-5,716,817	02-10-1998	T?rnell	
	44	US-6,140,552	10-31-2000	Deboer et al.	
	45	US-2003/0163836	08-28-2003	Garofalo et al.	
	46	US-2002/0194625	12-19-2002	Zcharia et al.	
	47	US-6,190,875	02-20-2001	Ben-Artzi et al.	
	48	US-2001/0006630	05-5-2001	Yacobi-Zeevi et al.	
	49	US-2002/0114801	08-22-2002	Pecker et al.	
	50	US-6,475,763	05-5-2002	Ayal-Hershkovitz et al.	
	51	US-6,426,209	07-30-2002	Ayal-Hershkovitz et al.	
	52	US-2002/0168749	11-14-2002	Pecker et al.	
	53	US-2003/0068806	04-10-2003	Ayal-Hershkovitz et al.	
	54	US-2003/0031660	02-13-2003	Yacobi-Zeevi et al.	
	55	US-4,859,581	08-22-1989	Nicholson et al.	
	56	US-4,882,318	11-21-1989	Vlodavsky et al.	
	57	US-5,129,877	07-14-1992	Gallo et al.	
	58	US-5,206,223	04-27-1993	Vlodavsky et al	
	59	US-5,332,812	07-26-1994	Nicolson et al.	
	60	US-5,362,641	08-8-1994	Fulks et al.	
	61	US-5,399,351	03-21-1995	Leshchner et al	
	62	US-5,550,116	08-27-1996	Lormeau et al.	
	63	US-5,667,501	09-16-1997	Fowler et al.	
	64	US-5,739,115	04-14-1998	Fugedi et al	
	65	US-6,348,344	02-19-2002	Ayal-Hershkovitz et al.	
/MD/	66	US-4,946,778	08-8-1990	Ladner et al.	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant.<sup>1</sup> Applicant's unique citation designation number (optional).<sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

\* For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.<sup>4</sup> Kind of document by the two-letter symbols as indicated on the document under WIPO Standard ST. 16 if possible.<sup>5</sup> Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.07 and 1.08. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

/Marianne Dibrino/

03/13/2008

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 3 of 23

Complete if Known

Application Number	10/645,659
Filing Date	August 22, 2003
First Named Inventor	Oron YACOBY-ZEEVI et al
Art Unit	1644
Examiner Name	DIBRINO, MARIANNE NMN

Attorney Docket Number 26128

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Documents	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/MD/	67	PCT WO 95/04158	09-9-1995	Hoogewerf et al.	T
	68	PCT WO 99/21975	06-6-1999	Freeman et al.	
	69	PCT WO 91/19197	12-12-1991	Nicolson et al.	
	70	PCT WO 95/04518	02-16-1995	Midha et al.	
	71	PCT WO 03/006645 A2	01-23-2003	Bohlen et al.	
	72	PCT WO 97/11684	03-3-1997	Bennett et al.	
	73	PCT WO 99/18852	04-22-1999	Arenson	
	74	PCT WO 91/02977	07-7-1991	Fuks et al.	
	75	PCT WO 97/27327	07-31-1997	Van Ness et al.	
	76	PCT WO 00/52149	08-8-2000	Yacobi-Zeevi	
	78	PCT WO 00/52178	08-8-2000	Pecker et al.	
	79	PCT WO 99/40207	08-12-1999	Nakajima et al.	
	80	PCT WO 98/46258	10-22-1998	Bhaskar et al.	
	81	EP 0254067	01-27-1988	Cohen et al.	
	82	PCT WO 98/03638	01-29-1998	Freeman et al.	
	83	PCT WO 01/00643	04-4-2001	Pecker et al.	
	84	PCT WO 99/48478	09-30-1999	Yacobi-Zeevi	
	85	PCT WO 00/03036	01-20-2000	Ben-Artzi et al.	
	86	PCT WO 00/25817	05-11-2000	Peretz et al.	
	87	PCT WO 92/01003	01-23-1992	Nicolson et al.	
	88	PCT WO 02/32283	04-25-2002	Yacobi-Zeevi	
	89	PCT WO 02/19962	03-14-2002	Ilan et al.	
/MD/	90	AU 735110	06-26-2001	Pecker et al.	
/MD/	91	PCT WO 99/57244	11-11-1999	Ben-Artzi et al.	
	92	PCT WO 99/57153	11-11-1999	Pecker et al.	
	93	PCT WO 99/11798	03-11-1999	Pecker et al.	
/MD/	94	PCT WO 88/01280	02-25-1988	Nicolson et al.	

Examiner Signature	Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant.<sup>1</sup> Applicant's unique citation designation number (optional).<sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04.<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

\* For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.<sup>1</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.<sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	4	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			T <sup>2</sup>
/MD/	95	Vlodavsky et al. "Morphological Appearance, Growth Behaviour and Migratory Activity of Human Tumor Cells Maintained on Extracellular Matrix Versus Plastic", Cell, 19: 607-616, 1980.	abstract		
	96	Miao et al. "Modulation of Fibroblast Growth Factor-2 Receptor Binding Dimerization, Signaling, and Angiogenic Activity by A Synthetic Heparin-Mimicking Polyaromatic Compound", J. Clin. Invest., 99(7): 1565-1575, 1997.	abstract		
	97	Raghunath et al. "Cultured Epithelial Autografts: Diving From Surgery Into Matrix Biology", Pediatr. Surg. Int., 12(7): 478-483, 1997. Abstract.	abstract		
	98	Maillard et al. "Pre-Treatment With Elastase Improves the Efficiency of Percutaneous Adenovirus-Mediated Gene Transfer to the Arterial Media", Gene Therapy, 5: 1023-1030, 1998.	abstract		
	99	Wang "Basic Fibroblast Growth Factor for Stimulation of Bone Formation in Osteoinductive or Conductive Implants", Acta Orthop. Scand. Suppl., 269: 1-33, 1996. Abstract.	abstract		
	100	Wang "Basic Fibroblast Growth Factor Infused at Different Times During Bone Graft Incorporation. Titanium Chamber Study in Rats", Acta Orthop. Scand., 67(3): 229-236, 1996. Abstract.	abstract		
	101	Aspenberg et al. "Fibroblast Growth Factor Stimulates Bone Formation, Bone Induction Studied in Rats", Acta Orthop. Scand., 60(4): 473-476, 1989. Abstract.			
	102	Aspenberg et al. "Dose-Dependent Stimulation of Bone Induction by Basic Fibroblast Growth Factor in Rats", Acta Orthop. Scand., 62(5): 481-484, 1991. Abstract.			
	103	Matoba et al. "Evaluation of Omental Implantation for Perforated Gastric Ulcer Therapy: Findings in A Rat Model", J. Gastroenterol., 31(6): 777-784, 1996. Abstract.			
	104	Aplin "Adhesion Molecules in Implantation", Reviews of Reproduction, 2(2): 84-93, 1997.			
	105	Lessey et al. "Paracrine Signaling in the Endometrium: Integrins and the Establishment of Uterine Receptivity", J. Reprod. Immunol., 39(1-2): 105-116, 1998. Abstract.			
	106	Burrows et al. "Trophoblast Migration During Human Placental Implantation", Hum. Reprod. Update, 2(4): 307-321, 1996.			
	107	Bischof et al. "The Regulation of Endometrial and Trophoblastic Metalloproteinases During Blastocyst Implantation", Contracept Fertil Sex, 22(1): 48-51, 1994. Abstract. <i>Article in French.</i>			
/MD/	108	Smits et al. "Expression of Heparan Sulfate Proteoglycan (Perlecan) in the Mouse Blastocyst Is Regulated During Normal and Delayed Implantation", Dev. Biol., 184(1): 38-47, 1997. Abstract.			

<sup>1</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>2</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

/Marianne Dibrino/

03/13/2008

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	5	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	109	Abrahamsohn et al. "Implantation and Decidualization in Rodents", <i>J. Exp. Zool.</i> , 266(6): 603-628, 1993. Abstract.			
	110	Yoshida "Effects of Basic Fibroblast Growth Factor on the Development of Mouse Preimplantation Embryos", <i>Nippon Sanka Fujinka Gakkai Zasshi</i> , 48(3): 170-176, 1996. Abstract.			
	111	Watson et al. "A Growth Factor Phenotype Map for Ovine Preimplantation Development", <i>Biology of Reproduction</i> , 50(4): 725-733, 1994. Abstract.			
	112	Carlone et al. "Embryonic Modulation of Basic Fibroblast Growth Factor in the Rat Uterus", <i>Biology of Reproduction</i> , 49(4): 653-665, 1993.			
	113	Wordinger et al. "The Immunolocalization of Basic Fibroblast Growth Factor in the Mouse Uterus During the Initial Stages of Embryo Implantation", <i>Growth Factors</i> , 11(3): 175-186, 1994. Abstract.			
	114	Schultz et al. "Growth Factors in Preimplantation Mammalian Embryos", <i>Oxford Review of Reproduction in Biology</i> , 15: 43-81, 1993. Abstract.			
	115	Richardson et al. "Regulation of Basic Fibroblast Growth Factor Binding and Activity by Cell Density and Heparan Sulfate", <i>J. Biological Chemistry</i> , 274(19): 13534-13540, 1990.			
	116	Hayward et al. "Cellular Mechanisms of Heparinase III Protection in Rat Traumatic Shock", <i>American Journal of Physiology</i> , 275: H23-H30, 1998.			
	117	Sasisekharan et al. "Heparinase Inhibits Neovascularization", <i>Proc. Natl. Acad. Sci. USA</i> , 91: 1524-1528, 1994.			
	118	Whitelock et al. "The Degradation of Human Endothelial Cell-Derived Perlecan and Release of Bound Basic Fibroblast Growth Factor by Stromelysin, Collagenase, Plasmin, and Heparanases", <i>Journal of Biological Chemistry</i> , 271(17): 10079-10086, 1996.			
	119	Godder et al. "Heparanase Activity in Cultured Endothelial Cells", <i>Journal of Cellular Physiology</i> , 148: 274-280, 1991.			
	120	Kato et al. "Physiological Degradation Converts the Soluble Syndecan-1 Ectodomain From An Inhibitor to A Potent Activator of FGF-2", <i>Nature Medicine</i> , 4(6): 691-697, 1998.			
	121	Jin et al. "Immunochemical Localization of Heparanase in Mouse and Human Melanomas", <i>International Journal of Cancer</i> , 45: 1088-1095, 1990.			
	122	Oldberg et al. "Characterization of A Platelet Endoglycosidase Degrading Heparin-Like Polysaccharides", <i>Biochemistry</i> , 19: 5755-5762, 1980.			
/MD/	123	Miyake et al. "Highly Specific and Sensitive Detection of Malignancy in Urine Samples From Patients With Urothelial Cancer by CD44v8-10/CD44v10 Competitive RT-PCR", <i>Int. J. Cancer</i> , 79(6): 560-564, 1998. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. \*Applicant's unique citation designation number (optional). \*See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>1</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>2</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. \*Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>3</sup>Applicant is to place a check mark here if English language Translation is attached.

This form is not a patent application. The information is required to obtain or retain a benefit by the public which is to be filed (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14, this collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

Complete if Known

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet	6	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	124	Kang et al. "Prolactin-Inducible Enhancer Activity of the First Intron of the Bovine $\beta$ -Casein Gene", <i>Mol. Cells</i> , 8(3): 259-265, 1998. Abstract.			
	125	Gottschalk et al. "Somatic Gene Therapy: Present Situation and Future Perspective", <i>Arzneimittelforschung</i> , 48(11): 1111-1120, 1998. Abstract.			
	126	Guriee et al. "CD44 Isoforms With Exon V6 and Metastasis of Primary N0M0 Breast Carcinomas", <i>Breast Cancer Res. Treat.</i> , 44(3):261-268, 1997. Abstract.			
	127	Vladovsky et al. "Mammalian Heparanase: Gene Cloning, Expression and Function in Tumor Progression and Metastasis", <i>Nature Medicine</i> , 5(7): 793-802, 1999			
	128	Faber-Elman et al. "Involvement of Wound-Associated Factors in Rat Brain Astrocyte Migratory Response to Axonal Injury: In Vitro Simulation", <i>J. Clin. Invest.</i> , 97(1): 162-171, 1996.			
	129	Zheng et al. "Increment of hF1X Expression With Endogenous Intron 1 In Vitro", <i>Cell Res.</i> , 7(1):21-29, 1997 Abstract.			
	130	Welch et al. "Expression of Ribozymes in Gene Transfer Systems to Modulate Target RNA Levels", <i>Cur. Opin. Biotechnol.</i> , 9(5): 486-496, 1998. Abstract.			
	131	Gewirtz et al. "Facilitating Oligonucleotide Delivery: Helping Antisense Deliver on Its Promise", <i>Proc. Natl. Acad. Sci. USA</i> , 93: 3161-3163, 1996.			
	132	Green et al. "Antisense Oligonucleotides: An Evolving Technology for the Modulation of Gene Expression in Human Disease", <i>Journal of American Cell Surgery</i> , 191(1): 93-105, 2000.			
	133	Agrawal "Antisense Oligonucleotides: Towards Clinical Trials", <i>TIBTech</i> , 14: 376-387, 1996.			
	134	Rajur et al. "Covalent Protein-Oligonucleotide Conjugates for Efficient Delivery of Antisense Molecules", <i>Bioconjugate Chem.</i> , 8: 935-940, 1997.			
	135	Luft "Making Sense Out of Antisense Oligodeoxynucleotide Delivery: Getting There Is Half the Fun", <i>J. Mol. Med.</i> , P.75-76, 1998.			
	136	Kronenwett et al. "Oligodeoxynucleotide Uptake in Primary Human Hematopoietic Cells Is Enhanced by Cationic Lipids and Depends on the Hematopoietic Cell Subset", <i>Blood</i> , 91(3): 852-862, 1998.			
	137	Flanagan et al. "Potent and Selective Gene Inhibition Using Antisense Oligodeoxynucleotides", <i>Molecular and Cellular Biochemistry</i> , 172: 213-225, 1997.			
	138	Aoki et al. "In Vivo Transfer Efficiency of Antisense Oligonucleotides Into the Myocardium Using HVJ-Liposome Method", <i>Biochemical and Biophysical Research Communications</i> , 231: 540-545, 1997.			
↓	139	Jayaraman et al. "Rational Selection and Quantitative Evaluation of Antisense Oligonucleotides", <i>Biochimica et Biophysica Acta</i> , 1520: 105-114, 2001.			
/MD/	140	Walton et al. "Prediction of Antisense Oligonucleotide Binding Affinity to A Structured RNA Target", <i>Biotechnology and Bioengineering</i> , 65(1): 1-9, 1999.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.4. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup>For Japanese patent documents, the indication of the year or the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Complete if Known

<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>		Application Number	10/645,659
		Filing Date	August 22, 2003
		First Named Inventor	Oron YACOBY-ZEEVI et al
		Group Art Unit	1644
		Examiner Name	DIBRINO, MARIANNE NMN
Sheet	7	of	23
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	
/MD/	141	Wang et al. "Isolation and Characterization of <i>Pseudomonas Aeruginosa</i> Genes Inducible by Respiratory Mucus Derived From Cystic Fibrosis Patients", Mol. Microbiol., 22(5): 1005-1012, 1996. Abstract.	
	142	Davies et al. "Regulation of the Alginate Biosynthesis Gene <i>AlgC</i> in <i>Pseudomonas Aeruginosa</i> During Biofilm Development in Continuous Culture", Appl. Environ. Microbiol., 61(3): 860-867, 1995. Abstract.	
	143	Azghani et al. "A Beta-Linked Mannan Inhibits Adherence of <i>Pseudomonas Aeruginosa</i> to Human Lung Epithelial Cells", Glycobiology, 5(1): 39-44, 1995. Abstract.	
	144	Ofek et al. "Bacterial Adhesion to Cells and Tissues", Chapman & Hall, NY, P.114-118, 148-153, 418-423, 420-423, 1994.	
	145	Ghani et al. "Ceftazidime, Gentamicin, and Rifampicin in Combination, Kill Biofilms of Mucoid <i>Pseudomonas Aeruginosa</i> ", Can. J. Microbiol., 43(11): 999-1004, 1997. Abstract.	
	146	Gabriel et al. "In Vitro Adherence of <i>Pseudomonas Aeruginosa</i> to Four Intraocular Lenses", J. Cataract Refract Surg., 24: 124-129, 1998. abstract	
	147	Pier "Rationale for Development of Immunotherapies That Target Mucoid <i>Pseudomonas Aeruginosa</i> Infection in Cystic Fibrosis Patients", Behring Inst. Mitt., 98: 350-360, 1997. Abstract.	
	148	Hatano et al. "Biologic Activities of Antibodies to the Neutral-Polysaccharide Component of the <i>Pseudomonas Aeruginosa</i> Lipopolysaccharide Are Blocked by O Side Chains and Mucoid Exopolysaccharide (Alginate)", Infect. Immun., 63(1): 21-26.	
	149	Melulemi et al. "Mucoid <i>Pseudomonas Aeruginosa</i> Growing in A Biofilm In Vitro Are Killed by Opsonic Antibodies to the Mucoid Exopolysaccharide Capsule But Not by Antibodies Produced During Chronic Lung Infection in Cystic Fibrosis Patients", J. Immun., 155(4): 2029-2038, 1995. Abstract.	
↓	150	Vernet et al. "Virulence Factors (Aerobactin and Mucoid Phenotype) in <i>Klebsiella Pneumoniae</i> and <i>Escherichia Coli</i> Blood Culture Isolates", FEMS Microbiol. Lett., 130(1): 51-57, 1995. Abstract.	
/MD/	151	Pier et al. "How Mutant CFTR May Contribute to <i>Pseudomonas Aeruginosa</i> Infection in Cystic Fibrosis", Am. J. Respir. Crit. Care Med., 154(4): S175-S182, 1996. Abstract.	

**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

/Marianne Dibrino/

03/13/2008

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Complete if Known

Application Number	10/645,659
Filing Date	August 22, 2003
First Named Inventor	Oron YACOBY-ZEEVI et al
Group Art Unit	1644
Examiner Name	DIBRINO, MARIANNE NMN

Sheet	8	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	152	Pier et al. "Cystic Fibrosis Transmembrane Conductance Regulator Is An Epithelial Cell Receptor for Clearance of Pseudomonas Aeruginosa From the Lung", Proc. Natl. Acad. Sci. USA, 94(22): 12088-12093, 1997.			
	153	Boucher et al. "Mucoid Pseudomonas Aeruginosa in Cystic Fibrosis: Characterization of Muc Mutations in Clinical Isolates and Analysis of Clearance in A Mouse Model of Respiratory Infection", Infect. Immun., 65(9): 3838-3846, 1997. Abstract.			
	154	Boucher et al. "Two Distinct Loci Affecting Conversion to Mucoidy Pseudomonas Aeruginosa in Cystic Fibrosis Encode Homologs of the Serine Protease HtrA", J. Bacteriol., 178(2): 511-523, 1996. Abstract.			
	155	Yu et al. "Microbial Pathogens in Cystic Fibrosis: Pulmonary Clearance of Mucoid Pseudomonas Aeruginosa and Inflammation in A Mouse Model of Repeated Respiratory Challenge", Infection and Immunity, 66(1): 280-288, 1998.			
	156	Van Heeckeren et al. "Excessive Inflammatory Response of Cystic Fibrosis Mice to Bronchopulmonary Infection With Pseudomonas Aeruginosa", J. Clin. Invest., 100(11): 2810-2815, 1997.			
	157	Cai et al. "Comparison of Sputum Processing Techniques in Cystic Fibrosis", Pediatr. Pulmonol., 22(6): 402-407, 1996. Abstract.			
	158	Hatch et al. "Alginate Lyase Promotes Diffusion of Aminoglycosides Through the Extracellular Polysaccharide of Mucoid Pseudomonas Aeruginosa", Antimicrob. Agents. Chemother., 42(4): 974-977, 1998. Abstract.			
	159	Speert et al. "Modulation of Macrophage Function for Defense of the Lung Against Pseudomonas Aeruginosa", Behring Inst. Mitt., 98: 274-282, 1997. Abstract.			
	160	Pina et al. "The Role of Fluoroquinolones in the Promotion of Alginate Synthesis and Antibiotic Resistance in Pseudomonas Aeruginosa", Curr. Microbiol., 35(2): 103-108, 1997. Abstract.			
	161	Mengistu et al. "Continuous Culture Studies on the Synthesis of Capsular Polysaccharide by Klebsiella Pneumoniae K1", J. Appl. Bacteriol., 76(5): 424-430, 1994. Abstract.			
↓	162	Hsueh et al. "Invasive Streptococci Pneumoniae Infection Associated With Rapidly Fatal Outcome in Taiwan", J. Formos Med. Assoc., 95(5): 364-371, 1996. Abstract.			
/MD/	163	Moses et al. "Relative Contributions of Hyaluronidase Capsule and M Protein to Virulence in A Mucoid Strain of the Group A Streptococcus", Infect. Immun., 65(1): 64-71, 1997.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup>Applicant's <sup>2</sup>reque citation designation number (optional). <sup>3</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 601.04. <sup>4</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>5</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>6</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>7</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application to the USPTO. This will vary depending on the complexity of the patent application. The burden on the applicant of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Complete if Known

<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)		Application Number	10/645,659	
		Filing Date	August 22, 2003	
		First Named Inventor	Oron YACOBY-ZEEVI et al	
		Group Art Unit	1644	
		Examiner Name	DIBRINO, MARIANNE NMN	
Sheet	9	of	23	
			Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>				
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		
/MD/	164	Scott et al. "Visualization of An Extracellular Mucoid Layer of <i>Treponema Denticola</i> ATCC 35405 and Surface Sugar Lectin Analysis of Some <i>Treponema</i> Species", <i>Oral Microbiol. Immunol.</i> , 12(2): 121-125, 1997. Abstract.		
	165	Nilsson et al. "The Role of Staphylococcal Polysaccharide Microcapsule Expression in Septicemia and Septic Arthritis", <i>Infect. Immun.</i> , 65(10): 4216-21, 1997. Abstract.		
	166	Wessels et al. "Effects on Virulence of Mutations in A Locus Essential for Hyaluronic Acid Capsule Expression in Group A Streptococci", <i>Infect. Immun.</i> , 62(2): 433-441, 1994. Abstract		
	167	Farndale et al. "A Direct Spectrophotometric Microassay for Sulfated Glycosaminoglycans in Cartilage Cultures", <i>Connective Tissue Research</i> , 9: 247-248, 1982.		
	168	Pasquier et al. "Implication of Neutral Polysaccharides Associated to Alginate in Inhibition of Murine Macrophage Response to <i>Pseudomonas Aeruginosa</i> ", <i>FEMS Microbiol. Lett.</i> , 147(2): 195-202, 1997. Abstract.		
	169	Marty et al. "Influence of Nutrient Media on the Chemical Composition of the Exopolysaccharide From Mucoid and Non-Mucoid <i>Pseudomonas Aeruginosa</i> ", <i>FEMS Microbiol. Letters</i> , 77(1-3): 35-44, 1992. Abstract.		
	170	Jorba et al. "Variations in the P. <i>Aeruginosa</i> Polysaccharide Synthesis Conditioned by Aminosugars", <i>Rev. Esp. Fisiol.</i> , 36(2): 155-161, 1980. Abstract.		
	171	Ramos et al. "Relationship Between Glycolysis and Exopolysaccharide Biosynthesis in <i>Lactococcus Lactis</i> ", <i>Appl. Environ. Microbiol.</i> , 67(1): 33-41, 2001. Abstract.		
	172	Bhaskar et al. "Dysregulation of Proteoglycan Production by Intrahepatic Biliary Epithelial Cells Bearing Defective (Delta-f508) Cystic Fibrosis Transmembrane Conductance Regulator", <i>Hepatology</i> , 27(1): 7-14, 1998. Abstract.		
	173	Vogel et al. "Production of Proteoglycans by Human Lung Fibroblasts (IMR-90) Maintained in A Low Concentration of Serum", <i>Biochem. J.</i> , 207(3): 369-379. Abstract.		
	174	Hill et al. "Organ-Specific Over-Sulfation of Glycosaminoglycans and Altered Extracellular Matrix in A Mouse Model of Cystic Fibrosis", <i>Biochem. Mol. Med.</i> , 62(1): 113-122, 1997. Abstract.		
/MD/	175	Welch et al. "Complex Saccharide Metabolism in Cystic Fibrosis Fibroblasts", <i>Pediatr. Research</i> , 9(9): 698-702, 1975.		

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>3</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 801.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet	10	of	23	Attorney Docket Number	26128
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	176	Rahmoune et al. "Chondroitin Sulfate in Sputum From Patients With Cystic Fibrosis and Chronic Bronchitis", Am. J. Resp. Cell & Mol. Biol., 5(4): 315-320, 1991. Abstract.			
	177	Beuth et al. "Lectin-Mediated Bacterial Adhesion to Human Tissue", Eur. J. Clin. Microbiol., 6(5): 591-593, 1987. Abstract.			
	178	Alison et al. "Polysaccharide Production in Pseudomonas Cepacia", J. Basic. Microbiol., 34(1): 3-10, 1994. Abstract.			
	179	Albus et al. "Staphylococcus Aureus Capsular Types and Antibody Response to Lung Infection in Patients With Cystic Fibrosis", J. Clin. Microbiol., 26(12): 2505-2509, 1988. Abstract.			
	180	Macone et al. "Mucoid Escherichia Coli in Cystic Fibrosis", The New England Journal of Medicine, 304(24): 1445-1449, 1981. Abstract.			
	181	Tatnall et al. "Characterisation of Alginates From Mucoid Strains of Pseudomonas Aeruginosa", Biochemical Society Transactions, 24: 404S, 1996.			
	182	Tatnall et al. "Chemical Analysis of Alginates From Mucoid Strains of Pseudomonas Aeruginosa", Biochemical Society Transactions, 22: 310S, 1994.			
	183	Tatnall et al. "Colonisation of Cystic Fibrosis Patients by Non-Mucoid Pseudomonas Aeruginosa - Characterisation of the Alginate From Mucoid Variants", Biochemical Society Transactions, 24: 406S, 1996.			
	184	Drigues et al. "Comparative Studies of Lipopolysaccharide and Exopolysaccharide From A Virulent Strain of Pseudomonas Solanacearum and From Three Avirulent Mutants", Journal of Bacteriology, 162(2): 504-509, 1985. Abstract.			
	185	Sutherland "Structure-Function Relationships in Microbial Exopolysaccharides", Biotech. Adv., 12: 393-448, 1994.			
	186	Anatolii "Hyaluronic Capsule as One of the Factors of Hemolytic Streptococcus- Pathogenicity", Chem. Abstracts 86(17): 339, 1977. Abstr.118714 in Zh. Mikrobiol. Epidemiol. Immunobiol., 2: 22-27, 1977.			
	187	Li et al. "Immunochemical Localization of Heparanase in Mouse and Human Melanomas", Int. J. Cancer, 45: 1088-1095, 1990.			
	188	Laskov et al. "Production of Heparanase by Normal and Neoplastic Murine - B-Lymphocytes", International Journal of Cancer, 47(1): 92-98, 1991.			
↓	189	Cordon-Carbo et al. "Expression of Basic Fibroblast Growth Factor in Normal Human Tissue", Laboratory Investigation, 63(6): 832-840, 1990. Abstract.			
/MD/	190	Hillier et al. "The WashU-Merck EST Project", No. N30824, Database GenBank on STN, US National Library of Medicine (Bethesda MD), 1996.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Complete if Known

Sheet	11	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
	191	Hillier et al. "The WashU-Merck EST Project", No. N30845, Database GenBank on STN, US National Library of Medicine (Bethesda MD), 1996.			
/MD/	192	Konstan et al. "Current Understanding of the Inflammatory Process in Cystic Fibrosis", Pediatric Pulmonology, 24: 137-142, 1997.			
	193	Dasgupta et al. "Reduction in Viscosity in Cystic Fibrosis Sputum In Vitro Using Combined Treatment With Nacystelyn and RhDNase", Pediatric Pulmonology, 22: 161-166, 1996. <b>Abstract</b>			
	194	Boat et al. "Biochemistry of Airway Mucus Secretions", Fed. Proc., 39(13): 3067-3074, 1980. Abstract.			
	195	Mohapatra et al. "Alteration of Sulfation of Glycoconjugates, But Not Sulfate Transport and Intracellular Inorganic Sulfate Content in Cystic Fibrosis Airway Epithelial Cells", Pediatric Res., 38(1): 42-48, 1995. Abstract.			
	196	Cheng et al. "Increased Sulfation of Glycoconjugates in Cultured Nasal Epithelial Cells From Patients With Cystic Fibrosis", J. Clin. Invest., 84(1): 68-72, 1989. Abstract.			
	197	Boat et al. "Epithelial Cell Dysfunction in Cystic Fibrosis: Implications for Airways Disease", Acta Paediatr. Scand. Suppl., 363: 25-29, 1989.			
	198	Schwartz et al. "CPG Motifs in Bacterial DNA Cause Inflammation in the Lower Respiratory Tract", J. Clin. Invest., 100(1): 68-73, 1997. Abstract.			
	199	Barghouthi et al. "Nonopsonic Phagocytosis of Pseudomonas Aeruginosa Requires Facilitated Transport of D-Glucosamine by Macrophages", J. Immunol., 154(7): 3420-3428, 1995. Abstract.			
	200	Moser et al. "Chronic Pseudomonas Aeruginosa Lung Infection Is More Severe in Th2 Responding BALB/c Mice Compared to Th1 Responding C3H/HeN Mice", APMIS, 105(11): 838-842, 1997. Abstract.			
	201	Zahm et al. "Early Alterations in Airway Mucociliary Clearance and Inflammation of the Lamina Propria in CF Mice", Am. J. Physiol., 272(3 Pt 1): C853-C859, 1997. Abstract.			
	202	Thompson et al. "Identification of Chondroitin Sulfate E in Human Lung Mast Cells", J. Immunol., 140(8): 2708-2713, 1988. Abstract.			
↓	203	Giuffrè et al. "Monocyte Adhesion to Activated Aortic Endothelium: Role of L-Selectin and Heparan Sulfate Proteoglycans", J. Cell Biol., 136(4): 945-956, 1999. Abstract.			
/MD/	204	Margolies et al. "Identification of A Major Heparin-Precipitable Protein in Human Serum and Its Relationship to Cystic Fibrosis", Pediatr. Res., 16(3): 181-186, 1982. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant.<sup>4</sup> Applicant's unique citation designation number (optional).<sup>5</sup> See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04.<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of year of the reign of the Emperor must precede the serial number of the patent document.<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Complete if Known

Application Number	10/645,659
Filing Date	August 22, 2003
First Named Inventor	Oron YACOBY-ZEEVI et al
Group Art Unit	1644
Examiner Name	DIBRINO, MARIANNE NMN

Sheet	12	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	205	Leong et al. "Different Classes of Proteoglycans Contribute to the Attachment of Borrelia Burgdorferi to Cultured Endothelial and Brain Cells", Infect. Immun., 66(3): 994-999, 1998. Abstract.			
	206	Asagon et al. "Effect of Heparin on Infection of Cells by Equine Arteritis Virus", J. Vet. Med. Sci., 59(8): 727-728, 1997. Abstract.			
	207	Krusat et al. "Heparin-Dependent Attachment of Respiratory Syncytial Virus (RSV) to Host Cells", Arch. Virol., 142(6): 1247-1254, 1997. Abstract.			
	208	Hagiwara et al. "Inhibitory Effect of Heparin on Red Blood Cell Invasion by Theileria Sergenti Merozoites", Int. J. Parasitol., 27(5): 535-539, 1997. Abstract.			
	209	Shakibaee et al. "Dual Interaction of the Malaria Circumsporozoite Protein With the Low Density Lipoprotein Receptor-Related Protein (LRP) and Heparan Sulfate Proteoglycans", J. Exp. Med., 184(5): 1699-1711, 1996. Abstract.			
	210	Jusa et al. "Effect of Heparin on Infection of Cells by Porcine Reproductive and Respiratory Syndrome Virus", Am. J. Vet. Res., 58(5): 488-491, 1997. Abstract.			
	211	Ganti et al. "Cell Adhesion to A Motif Shared by the Malaria Circumsporozoite Protein and Thrombospondin Is Mediated by Its Glycosaminoglycan-Binding Region and Not by CSVTG", J. Biol. Chem., 272(31): 19205-19213, 1997. Abstract.			
	212	Robert et al. "Chondroitin-4-Sulfatase (Proteoglycan), A Receptor for Plasmodium Falciparum-Infected Erythrocyte Adherence on Brain Microvascular Endothelial Cells", Res. Immunol., 146(6): 383-393, 1995. Abstract.			
/MD/	213	Berkow "The Merck Manual", Merck Research Laboratories, P.201, 204, 1308, 177-179, 1016-1017, 194-197, 885, 601, 1997.			
	214	Konstan et al. "Patterns of Medical Practice in Cystic Fibrosis: Part II. Use of Therapies", Pediatr. Pulmonol., 28(4): 248-54, 1999. Abstract.			
/MD/	215	Frederiksen et al. "Antibiotic Treatment of Initial Colonization with Pseudomonas Aeruginosa Postpones Chronic Infection and Prevents Deterioration of Pulmonary Function in Cystic Fibrosis", Pediatr. Pulmonol. 23(5): 330-335, 1997. Abstract.			
/MD/	216	Frederiksen et al. "Changing Epidemiology of Pseudomonas Aeruginosa Infection in Danish Cystic Fibrosis Patients (1974-1995)", Pediatr. Pulmonol., 28(3): 159-166, 1999. Abstract.			
/MD/	217	Ramsey et al. "Intermittent Administration of Inhaled Tobramycin in Patients With Cystic Fibrosis. Cystic Fibrosis Inhaled Tobramycin Study Group", New England Journal of Medicine, 340(1): 23-30, 1999. Abstract.			
/MD/	218	Tang et al. "Contribution of Specific Pseudomonas Aeruginosa Virulence Factors to Pathogenesis of Pneumonia in A Neonatal Mouse Model of Infection", Infect. Immun., 64(1): 37-43, 1996. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 601.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

Complete if Known

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	13	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	219	Bennett et al. "Effect of Uridine 5'-Triphosphate Plus Amiloride on Mucociliary Clearance in Adult Cystic Fibrosis", Am. J. Respir. Crit. Care Med., 153(6 Pt.1): 1796-1801, 1996. Abstract.			
	220	Armstrong et al. "Lower Airway Inflammation in Infants and Young Children With Cystic Fibrosis", Am. J. Respir. Crit. Care Med., 156(4 Pt.1): 1197-1204, 1997. Abstract.			
	221	Naparstek et al. "Activated T Lymphocytes Produce A Matrix-Degrading Heparan Sulphate Endoglycosidase", Nature, 310(5974): 241-244, 1984. Abstract.			
	222	Weller "Implications of Early Inflammation and Infection in Cystic Fibrosis: A Review of New and Potential Interventions", Pediatric Pulmonology, 24: 143-146, 1997.			
	223	Rubin "Emerging Therapies for Cystic Fibrosis Lung Disease", Chest, 115: 1120-1126, 1999.			
	224	Ducy et al. "The Osteoblast: A Sophisticated Fibroblast Under Central Surveillance", Science, 289: 1501-1504, 2000.			
	225	Reddi "Role of Morphogenetic Proteins in Skeletal Tissue Engineering and Regeneration", Nature Biotechnology, 16: 247-252, 1998.			
	226	Elkin et al. "Heparanase as Mediator of Angiogenesis: Mode of Action", The FASEB Journal, 15: 1661-1663, 2001.			
	227	Elkin et al. "Heparanase as Mediator of Angiogenesis: Mode of Action", The FASEB Journal, Published Online, 10 P. 2001.			
	228	Finkel "Potential Target Found for Antimetastasis Drugs", Science, 285: 33-34, 1999.			
	229	Webster et al. "FGFR Activation in Skeletal Disorders: Too Much of A Good Thing", TIG, 13(5): 178-182, 1997.			
	230	Shimazu et al. "Syndecan-3 and the Control of Chondrocyte Proliferation During Endochondral Ossification", Exp. Cell. Res., 229(1): 126-136, 1996. Abstract.			
	231	Blanquart et al. "CMDBS, Functional Analogs of Sulfate Heparanes, Used as Osseous Cicatrizing Agents", Ann. Endocrinol., 55(2): 121-123, 1994. Abstract.			
	232	Blanquart et al. "Heparan-Like Molecules Induce the Repair of Skull Defects", Bone, 17(6): 499-506, 1995. Abstract.			
	233	Muir et al. "Histomorphometric Analysis of the Effects of Standard Heparin on Trabecular Bone In Vivo", Blood, 88(4): 1314-1320, 1996. Abstract.			
	234	Hoffman et al. "Human Bone Morphogenic Protein 2 Contains A Heparin-Binding Site Which Modifies Its Biological Activity", Eur. J. Biochem., 237(1): 295-302, 1996. Abstract.			
/MD/	235	Imai et al. "Osteoblast Recruitment and Bone Formation Enhanced by Cell Matrix-Associated Heparin-Binding Growth-Associated Molecule (HB-GAM)", J. Cell. Biol., 143(4): 1113-1128, 1998. [Abstract]			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.57 and 1.66. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. The information is governed by 35 U.S.C. 122 and 37 CFR 1.14. The burden of collection is on the person to whom the information is requested to make reasonable efforts to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

Complete if Known

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	14	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published			
/MD/	236	Loredo et al. "Regulation of Glycosaminoglycan Metabolism by Bone Morphogenetic Protein-2 in Equine Cartilage Explant Cultures", Am. J. Vet. Res., 57(4): 554-559, 1996.			
/MD/	237	Kiberstis et al. "Bone Health in the Balance", Science, 289: 1497, 2000.			
	238	Scriwe "Tissue Engineers Build New Bone", Science, 289: 1498-1500, 2000.			
	239	Sreekanth et al. "Autotaxin, Tumor Metility Stimulating Exophosphodiesterase", Advan. Enzyme Regul., 37: 135-144, 1997. Introduction.			
/MD/	240	Bosi et al. "Antibodies Against A Peptide Sequence Within the HIV Envelope Protein Crossreact With Human Interleukin-2", Immunol. Invest., 17: 577-586, 1988.			
	241	Bendayan "Possibilities of False Immunocytochemical Results Generated by the Use of Monoclonal Antibodies: The Example of the Anti-Proinsulin Antibody", J. Histochem. Cytochem. 43: 881-886, 1995. Suppl. IDS in 22716;			
	242	Hillier et al. "The WashU-Merck EST Project" GenBank Entry N32056, 1996. Claims: 9-10, //			
	243	Adams et al. "Initial Assesment of Human Gene Diversity and Expression Patterns Based Upon 83 Million Nucleotides of cDNA Sequence", Nature, 377(6547): 3-174, 1995. GenBank Entry AA304653, 1997. Claims: 50-//			
	244	Yagel et al. "Normal Nonmetastatic Human Trophoblast Cells Share In Vitro Invasive Properties of Malignant Cells", J. Cellular Physiology, 136: 455-462, 1988.			
	245	Kizaki et al. "Cloning and Localization of Heparanase in Bovine Placenta", Placenta, 24: 424-430, 2003.			
	246	Dempsey et al. "Heparanase Expression in Invasive Trophoblasts and Acute Vascular Damage", Glycobiology, 10(5): 467-475, 2000. Abstract: P-470, Col.1 - P-471, Col.4, P-472, Col.1, § 1 Col.2, § 2.			
	247	Haimov-Kochman et al. "Localization of Heparanase in Normal and Pathological Human Placenta", Molecular Human Reproduction, 8(6): 566-573, 2002.			
	248	Kizaki et al. "Expression of Heparanase mRNA in Bovine Placenta During Gestation", Reproduction, 121: 573-580, 2001.			
	249	Edwards et al. "Some Properties and Applications of Monoclonal Antibodies", Biochem. Journal, 200: 1-10, 1981.			
/MD/	250	Zhou et al. "HFE Gene Knockout Produces Mouse Model of Hereditary Hemochromatosis", PNAS, 95(5): 2492-2497, 1998.			
	251	Menezo et al. "Mouse and Bovine Models for Human IVF", Reproductive BioMedicine Online 2002, 4(2): 170-175, 2002. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	15	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	252	Bean et al. "Fertilization In Vitro Increases Non-Disjunction During Early Cleavage Divisions In A Mouse Model System", Human Reproduction, 17(9): 2362-2367, 2002. Abstract.			
	253	Brinster et al. "Restoration of Fertility by Germ Cell Transplantation Requires Effective Recipient Preparation", Biology of Reproduction 69: 412-420, 2003. Abstract.			
	254	Liu et al. "Live Offspring by In Vitro Fertilization of Oocytes From Cryopreserved Primordial Mouse Follicles After Sequential In Vivo Transplantation and In Vitro Maturation", Biology of Reproduction, 64: 171-178, 2001. Abstract.			
	255	Kawase et al. "Effect of Partial Incision of the Zona Pellucida by Piezo-Micromanipulator for In Vitro Fertilization Using Frozen-Thawed Mouse Spermatozoa on the Developmental Rate of Embryos Transferred at the 2-Cell Stage", Biology of Reproduction, 66: 3810385, 2002. Abstract.			
	256	Praff et al. "Cryobiology of Rat Embryos I: Determination of Zygote Membrane Permeability Coefficients for Water and Cryoprotectants, Their Activation Energies, and the Development of Improved Cryopreservation Methods", Biology of Reproduction, 63: 1294-1302, 2000. Abstract.			
	257	Yesildaglar et al. "The Mouse as A Model to Study Adhesion Formation Following Endoscopic Surgery: A Preliminary Report", Human Reproduction, 14(1): 55-59, 1999. Abstract.			
	258	Ejima et al. "Induction of Apoptosis in Placentas of Pregnant Mice Exposed to Lipopolysaccharides: Possible Involvement of Fas/Fas Ligand System", Biology of Reproduction, 62: 178-185, 2000. Abstract.			
	260	Prchalada et al. "Diethylstilbestrol-Induced Cervical and Vaginal Adenosis Using the Neonatal Mouse Model", Biology of Reproduction, 38: 935-943, 1988. Abstract.			
	260	Newbold et al. "Exposure to Diethylstilbestrol During Pregnancy Permanently Alters the Ovary and Oviduct", Biology of Reproduction, 28: 735-744, 1983. Abstract.			
↓	261	Jin et al. "Molecular Cloning and Expression of Human Heparanase cDNA", Proceedings American Association for Cancer Research Annual Meeting, 1992, 33: 57, 1992. Abstract.			
/MD/	262	Ferber et al. "Pancreatic and Duodenal Homeobox Gene 1 Induces Expression of Insulin Genes in Liver and Ameliorates Streptozotocin-Induced Hyperglycemia", Nature Medicine, 6(5): 568-572, 2000.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant.<sup>3</sup> Applicant's unique citation designation number (optional).<sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.  
SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

/Marianne Dibrino/

03/13/2008

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet	16	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	263	Benjamini et al. "A Plasticity Window for Blood Vessel Remodelling Is Defined by Pericyte Coverage of the Preformed Endothelial Network and Is Regulated by PDGF-B and VEGF", Development, 125: 1591-1598, 1998			
	264	Vukicevic et al. "Induction of Nephrogenic Mesenchyme by Osteogenic Protein 1 (Bone Morphogenetic Protein 7)", Proc. Natl. Acad. Sci. USA, 93: 9021-9026, 1996.			
	265	Massague "The TGF-BETA Family of Growth and Differentiation Factors", Cell, 49: 437-438, 1987.			
	266	Pilbeam et al. "Comparison of the Effects of Various Lengths of Synthetic Human Parathyroid Hormone-Related Peptide (hPTHRP) of Malignancy on Bone Resorption and Formation in Organ Culture", Bone, 14: 717-720, 1993.			
	267	Skolnick et al. "From Genes to Protein Structure and Function: Novel Applications of Computational Approaches in the Genomic Era", Trends in Biotechnology, 18: 34-39, 2000.			
	268	Bork "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle", Genome Research, 10 : 398-400, 2000.			
	269	Doerks et al. "Protein Annotation: Detective Work for Function Prediction", Trends in Genetics, 14(6): 248-250, 1998.			
	270	Smith et al. "The Challenges of Genome Sequence Annotation or 'The Devil Is in the Details'", Nature Biotechnology, 15: 1222-1223, 1997.			
	271	Brenner "Errors in Genome Annotation", Trends in Genetics, 15(4): 132-133, 1999.			
	272	Bork "Go Hunting in Sequence Databases But Watch Out for the Traps", Trends in Genetics, 12(10): 425-427, 1996.			
	273	Bowie et al. "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions", Science, 247: 1306-1310, 1990.			
	274	Bendig et al. "Humanization of Rodent Monoclonal Antibodies by CDR Grafting", Methods in Enzymology, 8: 83-93, 1995			
	275	Coligan et al. "Current Protocols in Immunology", Immunology - Laboratory Manuals, 1991. <b>page 2.1.1-2.1.2</b>			
	276	Sasisekharan et al. "Cloning and Expression of Heparinase I Gene From Flavobacterium Heparinum", Proc. Natl. Acad. Sci. USA, 90: 3660-3664, 1993.			
	277	Cheng et al. "Increased Sulfation of Glycoconjugates NY Cultured Nasal Epithelia Cells From Patients With Cystic Fibrosis", Journal of Clinical Investigation, 84(1): 68-72, 1989. Abstract.			
	278	Carson et al. "Mucin and Proteoglycan Functions in Embryo Implantation", BioEssays, 20(7): 577-583, 1998. <b>Abstract, P. 580, Col 2, ¶ 2, P. 582, Col 1, Fig. 1, ¶ 1</b>			
/MD/	279	Novagen "PET System Manual", Novagen, 6th Ed., P.11, 1995.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 801.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	17	of	23	Attorney Docket Number	26128
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	280	Ennis et al. "Rapid Cloning of HLA-A, B cDNA by Using the Polymerase Chain Reaction: Frequency and Nature of Errors Produced in Amplification", PNAS USA, 87: 2833-2837, 1990.			
	281	Gilat et al. "Molecular Behaviour Adapts to Context: Heparanase Functions as An Extracellular Matrix-Degrading Enzyme or as A T-Cell Adhesion Molecule, Depending on the Local PH", Journal of Experimental Medicine, 181: 1929-1934, 1995.			
	282	Murphy et al. "The Latent Collagenase and Gelatin of Human Polymorphonuclear Neutrophil Leucocytes", Biochem. J., 192: 517-525, 1980.			
	283	Chubet et al. "Vectors for Expression and Secretion of FLAG Epitope-Tagged Proteins in Mammalian Cells", BioTechniques, 20: 136-141, 1996.			
	284	Chang et al. "Differential Ability of Heparan Sulfate Proteoglycans to Assemble the Fibroblast Growth Factor Receptor Complex In Situ", FASEB Journal, 14: 137-144, 2000.			
	285	Hillier et al. "The WashU-Merck EST Project", Database EMBL Accession No. N45367, XP 002198420, 1996. Abstract. <a href="#">View</a>			
	286	Marra et al. "The WashU-HHMI Mouse EST Project", Database EMBL, Accession No. AJ122034, XP 002198426, 1998. Abstract. <a href="#">View</a>			
	287	Marra et al. "The WashU-HHMI Mouse Est Project", Database EMBL, Accession No. AA047943, XP002198424, 1996.			
	288	Evans et al. "Human Chromosome 11 187a8 Cosmid, Complete Sequence", Database EMBL, Accession No. U73640, XP002198427, 1996. Abstract. <a href="#">View</a>			
	289	Suggs et al. "Use of Synthetic Oligonucleotides as Hybridization Probes: Isolation of Cloned cDNA Sequences for Human $\beta 2$ -Microglobulin", Proc. Natl. Acad. Sci. USA, 78(11): 6613-6617, 1981. <a href="#">View</a>			
	290	Ehle et al. "Immunoaffinity Chromatography of Enzymes", Bioseparation, 1(2): 97-110, 1990.			
↓	291	Nadav et al. "Activation, Processing and Trafficking of Extracellular Heparanase by Primary Human Fibroblasts", Journal of Cell Science, 115(10): 2179-2187, 2002.			
/MD/	292	Goldshmidt et al. "Cell Surface Expression and Secretion of Heparanase Markedly Promote Tumor Angiogenesis and Metastasis", Proc. Natl. Acad. Sci. USA, 99(15): 10031-10036, 2002.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST 3).

<sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.87 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

/Marianne Dibrino/

03/13/2008

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

Complete if Known

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	18	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	293	Guo et al. "Protein Tolerance to Random Amino Acid Change", PNAS, 101(25): 9205-9210, 2004.			
	294	Dibrino "RT-PCR Method & Applications", Clontech Laboratories, 1st Ed., 1: 11, 15, 23, 41, 26, 1991.			
	295	Zacharia et al. "Heparanase Regulates Murine Hair Growth", American Journal of Pathology, 166(4): 999-1008, 2005.			
	296	Zhu et al. "Development of Heritable Melanoma in Transgenic Mice", The Journal of Investigative Dermatology, 110: 247-252, 1998.			
	297	Duff "Transgenic Mice Overexpressing Presenilin cDNAs: Phenotype and Utility in the Modeling of Alzheimer's Disease", Central Nervous System Diseases, P.123-128, 2000. Abstract.			
	298	Doetschman "Interpretation of Phenotype in Genetically Engineered Mice", Laboratory Animal Science, 49(2): 137-143, 1999.			
	299	Wall "Transgenic Livestock: Progress and Prospects for the Future", Theriogenology, 45: 57-68, 1996.			
	300	Mullins et al. "Fulminant Hypertension in Transgenic Rats Harbouring the Mouse Ren-2 Gene", Nature, 344: 541-544, 1990.			
	301	Hammer et al. "Spontaneous Inflammatory Disease in Transgenic Rats Expressing HLA-B27 and Human <sup>32</sup> m: An Animal Model of HLA-B27-Associated Human Disorders", Cell, 63: 1099-1112, 1990.			
	302	Taurog et al. "HLA-B27 in Inbred and Non-Inbred Transgenic Mice", The Journal of Immunology, 141(11): 4020-4023, 1988.			
	303	Pearce et al. "Development of Glucose Intolerance in Male Transgenic Mice Overexpressing Human Glycogen Synthase Kinase-3 <sup>32</sup> on A Muscle-Specific Promoter", Metabolism, 53(10): 1322-1330, 2004.			
	304	Li et al. "In Vivo Fragmentation of Heparan Sulfate by Heparanase Overexpression Renders Mice Resistant to Amyloid Protein A Amyloidosis", PNAS, 102(18): 6473-6477, 2005.			
	305	Zacharia et al. "Heparanase Accelerates Wound Angiogenesis and Wound Healing in Mouse and Rat Models", The FASEB Journal, 19: 211-221, 2005.			
	306	Zacharia et al. "Molecular Properties and Involvement of Heparanase in Cancer Progression and Mammary Gland Morphogenesis", Journal of Mammary Gland Biology and Neoplasia, 6(3): 311-322, 2001.			
↓	307	Nadir et al. "Co- Interaction and Increased Release of Tissue Factor Pathway Inhibitor by Heparanase", Blood, 106(11/Part 2): 90B, 2005. Abstract# 4038.			
/MD/	308	Spiegel et al. "Heparanase Facilitates Development and SDF-1 Induced Migration of Hematopoietic Stem and Progenitor Cells", Blood, 102(11): 825a-826a, 2003. Abstract# 3056.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.4. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST 3).

<sup>4</sup>For Japanese patent documents, the indication of the year or the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.10. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P. O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	19	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	309	Zcharia et al. "Transgenic Expression of Mammalian Heparanase Uncovers Physiological Functions of Heparan Sulfate in Tissue Morphogenesis, Vascularization, and Feeding Behavior", The FASEB Journal, 18: 252-263, 2004.			
	310	Nasser et al. "Heparanase Neutralizes the Anticoagulant Properties of Heparin and Low-Molecular-Weight Heparin", Journal of Thrombosis and Haemostasis, 4: 560-565, 2006.			
	311	Mullins et al. "Expression of the DBA/2J Ren-2 Gene in the Adrenal Gland of Transgenic Mice", The EMBO Journal, 8(13): 4065-4072, 1989.			
	312	McKenzie et al. "Biochemical Characterization of the Active Heterodimer Form of Human Heparanase (Hpa1) Protein Expressed in Insect Cells", Biochemical Journal, 373: 423-435, 2003.			
	313	Ricoveri et al. "Heparan Sulfate Endoglycosidase and Metastatic Potential in Murine Fibrosarcoma and Melanoma", Cancer Research, 46(8): 3855-3861, 1986. Abstract.			
	314	Beneza et al. "Reversal of Fibroblast Growth Factor-Mediated Autocrine Cell Transformation by Aromatic Anionic Compounds", Cancer Research, 52: 5656-5662, 1992. <b>Abstract</b>			
	315	Irimura et al. "Chemically Modified Heparins as Inhibitors of Heparan Sulfate Specific Endo- $\beta$ -Glucuronidase (Heparanase) of Metastatic Melanoma Cells", Biochemistry, 25: 5322-5328, 1986. Abstract.			
	316	Coombe et al. "Analysis of the Inhibition of Tumor Metastasis by Sulphated Polysaccharides", Int. J. Cancer, 39: 82-88, 1987. Abstract.			
	317	Ornitz et al. "Heparin Is Required for Cell-Free Binding of Basic Fibroblast Growth Factor to A Soluble Receptor and for Mitogenesis in Whole Cells", Molecular and Cellular Biology, 12: 240-247, 1992.			
	318	Aviezer et al. "Differential Structural Requirements of Heparin and Heparan Sulfate Proteoglycans That Promote Binding of Basic Fibroblast Growth Factor to Its Receptor", J. Biol. Chem., 269(1): 114-121, 1994.			
	319	Bartlett et al. "Comparative Analysis of the Ability of Leucocytes, Endothelial Cells, and Platelets to Degrade the Subendothelial Basement Membrane: Evidence for Cytokine Dependence and Detection of A Novel Sulfatase", Immunology and Cell Biol., 73: 113-124, 1995.			
	320	Nakajima et al. "A Solid-Phase Substrate of Heparanase: Its Application to Assay of Human Melanoma for Heparan Sulfate Degrade Activity", Analytical Biochemistry, 157: 162-171, 1986.			
	321	Sewell et al. "Human Mononuclear Cells Contain An Endoglycosidase Specific for Heparan Sulfate Glycosaminoglycan Demonstrable With the Use of A Specific Solid-Phase Metabolically Radiolabelled Substrate", Biochem J., 264: 777-783, 1989.			
/MD/	322	Freeman et al. "A Rapid Quantitative Assay for the Detection of Mammalian Heparanase Activity", Biochemical Journal, 325: 229-237, 1997.			

EXAMINER: initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 801.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14 this collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	20	of	23	Attorney Docket Number	26128
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	323	Taylor et al. "A Colorimetric Method for the Quantitation of Uronic Acids and A Specific Assay for Galacturonic Acid", <i>Analytical Biochemistry</i> , 201: 190-196, 1992. <b>Abstract</b>			
	324	Basu et al. "Analysis of Glycosphingolipids by Fluorophore-Assisted Carbohydrate Electrophoresis Using Ceramide Glycanase From <i>Mercenaria mercenaria</i> ", <i>Analytical Biochemistry</i> , 222: 270-274, 1994. <b>Abstract</b>			
	325	Jackson "The Use of Polyacrylamide-Gel Electrophoresis for the High-Resolution of Separation of Reducing Sugars Labelled With the Fluorophore 8-Aminonaphthalene-1, 3, 6-Trisulphonic Acid", <i>Biochem J.</i> , 270: 705-713, 1990.			
	326	Matzner et al. "Degradation of Heparan Sulfate in the Subendothelial Extracellular Matrix by A Readily Released Heparanase From Human Neutrophils", <i>Journal of Clinical Investigation</i> , 76(4): 1306-1313, 1985.			
	327	Nakajima et al. "Heparanases and Tumor Metastasis", <i>Journal of Cellular Biochemistry</i> , 36(2): 157-167, 1988.			
	328	Ngo et al. "Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox", <i>The Protein Folding Problem and Tertiary Structure Prediction</i> , Birkhauser, Boston, P.433, 492-495, 1994.			
	329	Colman "Effects of Amino Acid Sequence Changes on Antibody-Antigen Interactions", <i>Research in Immunology</i> , 145(1): 33-36, 1994			
	330	Abaza et al. "Effects of Amino Acid Substitutions Outside An Antigenic Site on Protein Binding to Monoclonal Antibodies of Predetermined Specificity Obtained by Peptide Immunization: Demonstration With Region 94-100 (Antigenic Site 3) of Myoglobin", <i>Journal of Protein Chemistry</i> , 11(5): 433-444, 1992. <b>Abstract</b>			
	331	Lederman et al. "A Single Amino Acid Substitution in A Common African Allele of the CD4 Molecule Ablates Binding of the Monoclonal Antibody, OKT4", <i>Molecular Immunology</i> , 28: 1171-1181, 1991.			
	332	Li et al. " $\beta$ -Endorphin Omission Analogs: Dissociation of Immunoreactivity From Other Biological Activities", <i>PNAS</i> , 77: 3211-3214, 1980			
	333	Marchetti et al. "Neurotrophin Stimulation of Human Melanoma Cell Invasion: Selected Enhancement of Heparanase Activity and Heparanase Degradation of Specific Heparan Sulfate Subpopulations", <i>Cancer Research</i> , 56: 2856-2863, 1996. Also In: <i>Advances in Enzyme Regulation</i> , 37: 111-134, 1997.			
	334	Köhler et al. "Continuous Cultures of Fused Cells Secreting Antibody of Predefined Specificity", <i>Nature</i> , 256: 495-497, 1975.			
	335	Kussie et al. "Cloning and Functional Expression of A Human Heparanase Gene", <i>Biochemical and Biophysical Research Communication</i> , 261(1): 183-187, 1999.			
	336	Walch et al. "Correlation of Overexpression of the Low-Affinity p75 Neurotrophin Receptor With Augmented Invasion and Heparanase Production in Human Malignant Melanoma Cells", <i>Int. J. Cancer</i> , 82: 112-120, 1999.			
/MD/	337	Freeman et al. "Evidence That Platelet and Tumour Heparanases Are Similar Enzymes", <i>Biochem J.</i> , 342: 361-368, 1999.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with no communication to a applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

\* For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup>Kind of document by the approach of symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>5</sup>Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet	21	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	338	Zhou et al. "A 182 Bp Fragment of the Mouse Proα1(11) Collagen Gene Is Sufficient to Direct Chondrocyte Expression in Transgenic Mice", <i>J. Cell Science</i> , 108: 3677-3684, 1995.			
	339	Hormuzdi et al. "A Gene-Targeting Approach Identifies A Function for the First Intron in Expression of the α1 (I) Collagen Gene.", <i>Mol Cell Biol.</i> , 18(6): 3368-3375, 1998. Abstract.			
	340	Chow et al. "Development of An Epithelium-Specific Expression Cassette With Human DNA Regulatory Elements For Transgene Expression in Lung Airways", <i>Proc. Natl. Acad. Sci. USA</i> , 94: 14695-14700, 1997.			
	341	Ye et al. "Targeted Gene Correction: A New Strategy for Molecular Medicine", <i>Molecular Medicine Today</i> , P.431-437, 1998.			
	342	Lai et al. "Homologous Recombination Based Gene Therapy", <i>Exp. Nephrol.</i> , 7(1):11-14, 1999. Abstract.			
	343	Yazaki et al. "The Structure and Expression of the FGF Receptor-I mRNA Isoforms in Rat Tissues", <i>Biochimica et Biophysica Acta</i> , 1172: 37-42, 1993.			
	344	Le Fur et al. "Selective Increase in Specific Alternative Splice Variants of Tyrosinase in Murine Melanomas: A Projected Basis for Immunotherapy", <i>Proc. Natl. Acad. Sci. USA</i> , 94: 5332-5337, 1997.			
	345	Shastray "Gene Disruption in Mice: Models of Development and Disease", <i>Molecular and Cellular Biochemistry</i> , 181: 163-179, 1998.			
	346	Carpentier et al. "DNA Vaccination With HuD Inhibits Growth of A Neuroblastoma in Mice", <i>Clinical Cancer Research</i> , 4: 2819-2824, 1998.			
	347	Lai et al. "DNA Vaccines", <i>Critical Reviews in Immunology</i> , 18: 449-484, 1998.			
	348	Kurachi et al. "Role of Intron 1 in Expression of the Human Factor IX Gene", <i>Journal of Biological Chemistry</i> , 270(10): 5276-5281, 1995.			
	349	Shekhar et al. "Correlation of Differences in Modulation of Ras Expression With Metastatic Competence of Mouse Mammary Tumour Subpopulations", <i>Invasion Metastasis</i> , 14: 27-37, 1994/5.			
↓	350	Durand et al. "Active-Site Motifs of Lysosomal Acid Hydrolases: Invariant Features of Clan GH-A Glycosyl Hydrolases Deduced From Hydrophobic Cluster Analysis", <i>Glycobiology</i> , 7(2): 277-284, 1997.			
/MD/	351	Korb et al. "Stimulation of Gene Expression by Introns: Conversion of An Inhibitory Intron To A Stimulatory Intron by Alteration of the Splice Donor Sequence", <i>Nucleic Acids Research</i> , 21(25): 5901-5908, 1993.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.<sup>3</sup> Applicant's unique citation designation number (optional).<sup>4</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04.<sup>5</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. The time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be directed to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.  
SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Substitute for form 1449A/PTO

Complete if Known

**SUPPLEMENTAL INFORMATION  
DISCLOSURE  
STATEMENT BY APPLICANT**  
(use as many sheets as necessary)

Sheet	22	of	23	Attorney Docket Number	26128
<b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
/MD/	352	Linhardt et al. "Polysaccharide Lyases", Applied Biochemistry and Biotechnology, 12: 135-176, 1986.			
	353	Dempsey et al. "Heparanase, A Potential Regulator of CellMatrix Interactions", TIBS, 25(8): 349-351, 2000. P.350, Col.1, § 1, Col.3, § 1, Claims 1-24. <i>¶</i>			
	354	Niwa et al. "Efficient Selection for High-Expression Transfectants With A Novel Eukaryotic Vector", Gene, 108(2): 193-199, 1991. Abstract.			
	355	Mirault et al. "Transgenic Glutathione Peroxidase Mouse Models for Neuroprotection Studies", Ann. NY Acad. Sci., 738: 104-115, 1994. Abstract.			
	356	Lampard et al. "Secretion of Foreign Protein Mediated by Chicken Lysozyme Gene Regulatory Sequences", Biochem. Cell Biol., 80(6): 777-788, 2002. Abstract.			
	357	Morrison et al. "Sequences in Antibody Molecules Important for Receptor-Mediated Transport Into the Chicken Egg Yolk", Mol. Immunol., 38(8): 619-625, 2002. <i>Abstract</i>			
	358	Richards et al. "Construction and Preliminary Characterization of the Rat Casein and Alpha-Lactalbumin cDNA Clones", J. Biol. Chem., 256(1): 526-32, 1981.			
	359	Campbell et al. "Comparison of the Whey Acidic Protein Genes of the Rat and Mouse", Nucleic Acids Res., 12(22): 8685-8697, 1984.			
	360	Gorodetsky et al. "Isolation and Characterization of the Bos Taurus $\beta$ -Casein Gene", Gene, 66: 87-96, 1988. Abstract.			
	361	Benezra et al. "Thrombin Enhances the Degradation of Heparan Sulfate in the Extracellular Matrix by Tumor Cell Heparanase", Exptl. Cell. Res., 201: 208-215, 1992.			
	362	Harlow et al. "Antibodies - A Laboratory Manual", Cold Spring Harbor Press, P. 471-510, 1988.			
	363	Murray et al. "The Extracellular Matrix", Harper's Biochemistry, McGraw-Hill Professional, 24th Ed., Chap.57, P.667-685, 1998.			
	364	Selvan et al. "Heparan Sulfate in Immune Responses", Ann. NY Acad. Sci., 797: 127-139, 1996.			
↓/MD/	365	Prockop "Marrow Stromal Cells as Stem Cells for Nonhematopoietic Tissues", Science, 276: 71-74, 1997.			
	366	Pomahac et al. "Tissue Engineering of Skin", Crit. Rev. Oral Biol. Med., 9(3): 333-344, 1998. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.<sup>1</sup> Applicant's unique citation designation number (optional).<sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04.<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

/Marianne Dibrino/

03/13/2008

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature /Marianne Dibrino/ Considered 03/13/2008

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language

Translation is attached.  
Confidentiality of information is required by 37 CFR 1.107 and 1.108. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.  
SEND TO: Commissioner for Patents, P.O.



PTO/SB/08A (10-96)

Please type a plus sign (+) inside this box → +

Approved for use through 10/31/99 OMB 0651-0031

PATENT AND TRADEMARK OFFICE, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

---

**FOREIGN PATENT DOCUMENTS**

---

Examiner's Initials		Foreign Patent Documents			Name of Patentee or Applicant of Titled Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, columns, lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>1</sup>	Number <sup>2</sup>	Kind Code <sup>3</sup> (if known)				
/MD/	WO	03/006645		IMCLONE SYSTEMS INC.	01-23-2003			
Examiner Signature	/Marianne Dibrino/				Date 03/13/2008 Considered			

**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not used.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached *Kinds of U.S. Patent Document*. <sup>3</sup> Enter Office that issued the document by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese parent documents, the indication of the year of the reign of the Emperor must precede the serial number of the parent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 is possible. <sup>6</sup> Patent translation in another language than English. <sup>7</sup> Attached here if French language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: A lisant Commissioner for Oaths, 1400 14th Street, NW, Washington, DC 20004.

Please type a plus sign (+) inside this box → 

Approved for use through 10/31/99 OMB 0651-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no person is required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known

Application Number	10/456,573
Filing Date	06/09/2003
First Named Inventor	Iris PECKER
Group Art Unit	1646
Examiner Name	

Sheet	2	Of	2	Attorney Docket Number
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume/issue number(s), publisher, city and/or country where published.		T <sup>2</sup>
/MD/		Vlodavsky et al, "Inhibition of tumor metastasis by heparanase inhibiting species of heparin", <i>Invasion Metastasis</i> , 1994-95;14 (1-6):290-302 (abstract)		
		Parish et al, "Evidence that sulphated poly-醣 acids inhibit tumour metastasis by blocking tumour-cell-derived heparanases", <i>Int J Cancer</i> , 1987 Oct 15;40(4):511-8.		
		Lider et al, "Suppression of experimental autoimmune diseases and prolongation of allograft survival by treatment of animals with low doses of heparins", <i>J Clin Invest</i> , 1989 Mar;83(3):752-6.		
		Gewirtz et al, "Nucleic acid therapeutics: state of the art and future prospects", <i>Blood</i> , 1998 Aug 1;92(3):712-36.		
		Hida et al, "Antisense EIAF transfection restrains oral cancer invasion by reducing matrix metalloproteinase activities", <i>Am J Pathol</i> , 1997 Jun;150(6):2125-32 (abstract)		
		Thuong et al, "Sequence-specific recognition and modification of double-helical DNA by oligonucleotides", <i>Angew. Chem. Int. Ed. Engl.</i> , 32:666-690, 1993		
		Cohen, JS, "Oligonucleotide therapeutics", <i>Trends Biotechnol.</i> , 10(3):87-91, 1992 (abstract)		
		Szczylik et al, "Selective inhibition of leukemia cell proliferation by BCR-ABL antisense oligodeoxynucleotides", <i>Science</i> , 1991 Aug 2;253(5019):562-5. (abstract)		
		Calabretta et al, "Normal and leukemic hematopoietic cells manifest differential sensitivity to inhibitory effects of c-myc antisense oligodeoxynucleotides: an in vitro study relevant to bone marrow purging", <i>Proc Natl Acad Sci U.S.A.</i> 1991 Mar 15;88(6):2351-5.		
		Burch et al, "Oligonucleotides antisense to the interleukin 1 receptor mRNA block the effects of interleukin 1 in cultured murine and human fibroblasts and in mice", <i>J Clin Invest.</i> , 88(4):1190-1196, 1991 (abstract)		
		Agrawal S., "Antisense oligonucleotides as antiviral agents", <i>Trends Biotechnol.</i> , 10(5):152-158, 1992. (abstract)		
/MD/		Uno et al, "Antisense-mediated suppression of human heparanase gene expression inhibits pleural dissemination of human cancer cells", <i>Cancer Res.</i> 2001 Nov 1;61(21):7855-60.		
Examiner Signature	/Marianne Dibrino/			Date 03/13/2008 Considered

<sup>1</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>2</sup> Unique citation designation number. <sup>3</sup> Applicant is to place a check mark here if English language Translation is attached.

BUSENCE HOUR STATEMENT: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)

Atty. Docket No.  
910/1Application No  
08/922,170Applicant:  
Iris PECKER et alFiling Date:  
September 2, 1997RECEIVED  
GROUP 3  
1652  
S 98

## U.S. PATENT DOCUMENTS

	EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	700 CD00	FILING DATE
AA	RP	5,362,641	Nov 94	Fuks et al	465	205	
AB	RP	5,571,506	Nov 96	Regan et al	424	73,17	
AC							

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
							YES
AD	RP	WO 9504518	Jul 94	PCT	—	—	
AE							

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AF	RP	Goshen et al. "Purification and Characterization of Placental Heparanase and its Cultured Cytotrophoblasts", <i>Molecular Human Reproduction</i> , 2(9): 679-684, 1996	Expression by Matrix Heparan
AG	RP	Bar-Ner et al. "Inhibition of Heparanase-Mediated Degradation of Extracellular Sulphate by Non-anticoagulant Hepa in Species", <i>Blood</i> , 70(2): 551-557, 1987	
AH	RP	Savitsky et al. "Ataxia-Telangiectasia: Structural Diversity of Untranslated Sequences Suggests Complex Post-Transcriptional Regulation of ATM Gene Expression", <i>Nucleic Acids Research</i> , 25(9): 1678-1684 (1997)	
AI	RP	Haimovitz-Friedman et al. "Activation of Platelet Heparanase by Tumor Cell Derived Factors", <i>Blood</i> , 78: 789-796, 1991	
AJ	RP	Gospodarowicz et al. "Stimulation of Corneal Endothelial Cell Proliferation in vitro by Fibroblast and Epidemal Growth Factors", <i>Exp. Eye Res.</i> , 25: 75-89, 1977	
AK	RP	Ernst et al. "Enzymatic degradation of Glycosaminoglycans", <i>Crit. Rev. In Biochem. &amp; Molec. Biology</i> , 30(4): 387-444, 1995	
AL	RP	Zhong-Sheng et al. "Role of Heparan Sulfate Proteoglycans in the Binding and Uptake of A Polipoprotein E-enriched Remnant Lipoproteins by Cultured Cells", <i>J. Biol. Chem.</i> , 268(14): 10160-10167, 1993	
AM	RP	R. Ross. "The Pathogenesis of Atherosclerosis: A Perspective for the 1990s", <i>Nature</i> , 362: 801-809, (1993)	
AN	RP	1993Putnay et al. "A Putative Cellular Receptor for Dengue Viruses", <i>Nature Medicine</i> , 3(8): 828-829, 1997	
AO	RP	Cordon-Cardo et al. "Expression of Basic Fibroblast Growth Factor in Normal Human Tissues", <i>Laboratory Investigation</i> , 63(6): 832-840, 1990	

EXAMINER Rebecca Prouty DATE CONSIDERED 7-21-08

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)			Atty. Docket No. 910/1		Application No. 08/922,170		
INFORMATION DISCLOSURE CITATION IN AN APPLICATION (USE SEVERAL SHEETS IF NECESSARY)			Applicant: Iris PECKER et al		<i>RE/</i> <i>FER</i> <i>GROUP 11-1</i> <i>1652</i> <i>1800</i>		
			Filing Date: September 2, 1997		Group, v. 11-1		
U.S. PATENT DOCUMENTS							
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME		CLASS	SUB-CLASS	FILING DATE
BA							
FOREIGN PATENT DOCUMENTS							
	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION	
						YES	NO
BB							
OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)							
BC	RP	Narindrasorasak et al, "High Affinity Interactions between the Alzheimer's $\beta$ -Amyloid Precursor Proteins and the Basement Membrane Form of Heparan Sulfate Proteoglycan", <i>J. Biol. Chem.</i> , 266(20): 12878-12883, 1991					
BD	RP	Chen et al, "Dengue Virus Infectivity Depends on Envelope Protein B10 to Target Cell Heparan Sulfate", <i>Nature Medicine</i> , 3(8): 866-871, 1997					
BE	RP	Shieh et al, "Cell Surface Receptors for Herpes Simplex Virus are Heparan Sulfate Proteoglycan Proteoglycans", <i>J. Cell Biol.</i> , 116(5): 1277-1281, 1992					
BF	RP	Eisenberg et al, "Lipoprotein Lipase Enhances Binding of Lipoproteins to Heparan Sulfate on Cell Surfaces and Extracellular Matrix", <i>J. Clin. Invest.</i> , 90: 2013-2021, 1992					
BG	RP	Rapraeger et al, "Requirement of Heparan Sulfate for bFGF-Mediated Fibroblast Growth and Myoblast Differentiation", <i>Science</i> , 252: 1705-1708, 1991					
BH	RP	Lider et al, "A Disaccharide that Inhibits Tumor Necrosis Factor $\alpha$ is Formed from the Extracellular Matrix by the Enzyme Heparanase", <i>Proc. Natl. Acad. Sci. USA</i> , 92:5037-5041, 1995					
BI	RP	Lider et al, "Suppression of Experimental Autoimmune Diseases and Prolongation of Allograft Survival by Treatment of Animals with Low Doses of Heparins", <i>J. Clin. Invest.</i> , 83: 752-756, 1989					
BJ	RP	Gitay-Goren et al, "The Binding of Vascular Endothelial Growth Factor to its Receptors is Dependent on Cell Surface-associated Heparin-like Molecules", <i>J. Biol. Chem.</i> , 267(9): 6093-6098, 1992					
BK	RP	Ornitz et al, "FGF Binding and FGF Receptor Activation by Synthetic Heparin Derived Di- and Trisaccharides", <i>Science</i> , 268: 432-436, 1995.					
BL	RP	Spivak-Kroizman et al, "Heparin-Induced Oligomerization of FGF Molecules is Responsible for FGF Receptor Dimerization, Activation, and Cell Proliferation", <i>Cell</i> , 79: 1015-1024, 1994					
BM	RP	Xayon et al, "Cell Surface, Heparin-Like Molecules are required for Binding of Basic Fibroblast Growth Factor to its High Affinity Receptor", <i>Cell</i> , 64: 841-848, 1991					
BN							
EXAMINER <u>Rebecca Prouty</u>			DATE CONSIDERED <u>7-21-18</u>				
EXAMINER Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							

Form PTO-1449 (Modified)

Atty. Docket No.  
910/1Applicant No.  
08/922,717INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)Applicant:  
Iris PECKER et alFiling Date:  
September 2, 1997

Group 1st Unit:

16,52

RECEIVED  
FEB 2 1998  
GROUP 1800

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
CA						

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
CB						YES
						NO

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CC	RP	Vlodavsky et al, "Extracellular Matrix-Bound Growth Factors, Enzymes, and Plasminogen Proteins". Basic Membranes: Cellular and Molecular Aspects (eds. Rohrbach & Timpl) pp 327-343, Academic Press, Orlando, Fla., 1993
CD	RP	Vlodavsky et al, "Extracellular Sequestration and Release of Fibroblast Growth Factor: A Regulatory Mechanism?". <i>Trends Biochem. Sci.</i> , 16: 268-271, 1991
CE	RP	Ishai-Michaeli et al, "Heparanase Activity Expressed by Platelets, Neutrophils, and Lymphoma Cells Releases Active Fibroblast Growth Factor from Extracellular Matrix", <i>Cell Regulation</i> , 1: 833-842, 1990
CF	RP	Ishai-Michaeli et al, "Importance of Size and Sulfation of Heparin in Release of Active Fibroblast Growth Factor from the Vascular Endothelium and Extracellular Matrix", <i>Biochemistry</i> , 31(7): 2080-2088, 1992
CG	RP	Folkman et al, "A Heparin-Binding Angiogenic Protein - Basic Fibroblast Growth Factor is Stored Within Basement Membrane". <i>Am. J. Pathology</i> , 130(2): 393-400, 1988
CH	RP	Vlodavsky et al, "Endothelial Cell-Derived Basic Fibroblast Growth Factor: Synthesis and Deposition into Subendothelial Extracellular Matrix", <i>Proc. Natl. Acad. Sci. USA</i> , 84: 2292-2296, 1987
CI	RP	Folkman et al, "Angiogenic Factors", <i>Science</i> , 235: 442-447, 1987
CJ	RP	Burgess et al, "The Heparin-Binding (Fibroblast) Growth Factor Family of Proteins", <i>Annu. Rev. Biochem.</i> , 58:570-606, 1989
CK	RP	Vlodavsky et al, "Involvement of the Extracellular Matrix, Heparin Sulfate Proteoglycans, and Heparin Sulfate Degrading Enzymes in Angiogenesis and Metastasis", In: <i>Tumor Angiogenesis</i> , Eds. Lewis et al, Oxford Univ. Press, pp 125-140, 1997
CL	RP	Parise et al, "Evidence that Sulfated Polysaccharides Inhibit Tumor Metastasis by Blocking Tumor-Cell-Derived Heparanases", <i>Int. J. Cancer</i> , 40: 511-518, 1987
CM	RP	Bashkin et al, "Basic Fibroblast Growth Factor Binds to Subendothelial Extracellular Matrix and is Released by Heparanase and Heparin-Like Molecules", <i>Biochemistry</i> , 28: 1737-1743, 1989
CN		

EXAMINER Rebecca Pinty DATE CONSIDERED 7-21-98

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

Atty. Docket No.  
910/1Application No.  
08/117,720INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)Applicant:  
Iris PECKER et al

RECEIVED

FEB 9 1998

GROUP 1B

16:2 1500

Filing Date:  
September 2, 1997

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
DA						

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
DB						YES NO

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

DC	RP	Gospodarowicz et al, "Permissive effect of the ExtraCellular Matrix on Cell Proliferation <i>in vitro</i> ", <i>Proc. Natl Acad. Sci. USA</i> , 77(7): 4094-4098, 1980
DD	RP	Vlodavsky et al, "Morphological Appearance, Growth Behavior and Migratory Activity of Human Tumor Cells Maintained on ExtraCellular Matrix Versus Plastic", <i>Cell</i> , 19: 607-616, 1980
DE	RP	Vlodavsky et al, "Involvement of Heparanase in Tumor Metastasis and Angiogenesis", <i>Israel J. Med. Sci.</i> , 24: 464-470, 1988
DF	RP	Vlodavsky et al, "Lymphoma Cell-mediated Degradation of Sulfated Proteoglycan in the Subendothelial ExtraCellular Matrix: Relationship to Tumor Cell Metastasis", <i>Cancer Research</i> , 43: 2704-2711, 1983
DG	RP	Liotta et al, "Tumor Invasion and the ExtraCellular Matrix", <i>Lab. Inv.</i> , 49(6): 636-649, 1983
DH	RP	Nicolson, G.L., "Organ Specificity of Tumor Metastasis: Role of Preferential Adhesion, Invasion and Growth of Malignant Cells at Specific Secondary Sites", <i>Cancer Met. Rev.</i> , 7: 143-188, 1988
DI	RP	Nakajima et al, "Heparanases and Tumor Metastasis", <i>J. Cell. Biochem.</i> , 36: 157-167, 1988
DJ	RP	Vlodavsky et al, "Inhibition of Tumor Metastasis Inhibiting Species of Heparin", <i>Inv. Metast.</i> , 14: 290-302, 1994
	RP	Vlodavsky et al, "Expression of Heparanases by Platelets and Circulating Cells of the Immune System: Possible Involvement in Diapedesis and Extravasation", <i>Inv. Metast.</i> , 12: 112-127, 1992
	RP	Ruusulaiti et al, "Proteoglycans as Modulators of Growth Factor Activities", <i>Cell</i> , 64: 867-869, 1991
	RP	Kjellen et al, "Proteoglycans: Structures and Interactions", <i>Annu. Rev. Biochem.</i> , 50: 443-475, 1991
	RP	Wight, T.N., "Cell Biology of Arterial Proteoglycans", <i>Arteriosclerosis</i> , 9: 1-20, 1989
	RP	Jackson, et al, "Glycosaminoglycans: Molecular Properties, Protein Interactions, and Role in Physiological Processes", <i>Physiological Rev.</i> , 71(2): 481-539, 1991
	RP	Wight et al, "The Role of Proteoglycans in Cell Adhesion, Migration and Proliferation", <i>Curr. Opin. Cell Biol.</i> , 4: 793-801, 1992

EXAMINER Rebecca Ponty

DATE CONSIDERED

7-21-98

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)		JAN 05 2007		Atty Docket No.	Application No.		
PATENT & TRADEMARK OFFICE		SEARCHED		910/5	09/071,739		
INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (USE SEVERAL SHEETS IF NECESSARY)				RECEIVED	JUL 15 1998		
CANCELLATION		SEARCHED		Filing Date:	GROUP 1800		
SEARCHED		SEARCHED		May 1, 1998	SEARCHED		
PATENT DOCUMENTS							
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME		CLASS	SUB-CLASS	FILING DATE
AA							
FOREIGN PATENT DOCUMENTS							
	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION	
AB						YES NO	
OTHER ART (Including Author, Title, Date, Pernent Pages, Etc.)							
AC	MD	Wight et al, "The Role of Proteoglycans in Cell Adhesion, migration and Proliferation", <i>Current Opinion in Cell Biology</i> , 1992, 4:793-801					
AD	MD	Jackson et al, "Glycosaminoglycans: Molecular Properties, Protein Interactions, and Role in Physiological Processes", <i>Physiological Reviews</i> , 71(2):481-539, 1991					
AE	MD	Wight, T.N., "CellBiology of Arterial Proteoglycans", <i>Arteriosclerosis</i> , 9:1-20, 1989					
AF	MD	Kjellen et al, "Proteoglycans: Structures and Interactions", <i>Annu. Rev. Biochem.</i> , 60: 443-475, 1991					
AG	MD	Ruoslahti et al, "Proteoglycans as Modulators of Growth Factor Activities", <i>Cell</i> , 64:867-869, 1991					
AH	MD	Vlodavsky et al, "Extracellular Matrix-Bound Growth Factors, Enzymes and Plasma Protein", in <i>Basement Membranes: Cellular and Molecular Aspects</i> (eds.Rohrbach et al) pp 327-343, Academic Press Inc., Orlando, Fla.					
AI	MD	Vlodavsky et al, "Expression of Heparanas : by Platelets and Circulating Cells of the Immune System: Possible Involvement in Diapedesis and Extravasation", <i>Invasion &amp; Metastasis</i> , 12: 112-127, 1992					
AJ	MD	Vlodavsky et al, "Inhibition of Tumor Metastasis by Heparanase Inhibiting Species of Heparin", <i>Invasion &amp; Metastasis</i> , 14: 290-302, 1995					
AK	MD	Nakajima et al, "Heparanase and Tumor Metastasis", <i>J. Cell. Biochem.</i> , 36: 157-167, 1988					
AL	MD	Liotta et al, "Tumor Invasion and the Extracellular Matrix", <i>Lab. Invest.</i> , 49: 636-647, 1983					
AM	MD	Vlodavsky et al, "Lymphoma Cell Mediate Degradation of Sulfated Proteoglycans in the Subendothelial Extracellular Matrix: Relationship to Tumor Cell Metastasis", <i>Cancer Res.</i> , 43: 2704-2711, 1983					
AN	MD	Parish et al, "Evidence that Sulfated Polysaccharides Inhibit Tumor Metastasis by Blocking Tumor cell-Derived Heparanase", <i>Int. J. Cancer</i> , 40: 511-518, 1987					
AO	MD	Vlodavsky et al, "Morphological Appearance, Growth behavior and Migratory Activity of Human Tumor Cells Maintained on Extracellular Matrix vs. Plastic", <i>Cell</i> , 19: 607-616, 1980					
AP							
EXAMINER <i>Chris Dibari</i>				DATE CONSIDERED			7/12/99
Indicate, whether or not citation is in conformance with MPEP 609: Draw line through citation							

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form P-10-1449 (Modified)

Atty. Docket No.

Application No.  
09/071,739INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)Applicant:  
M. PECKER et alEfile Date:  
06/01/1998

Group Art Unit:

CANCELLLED

RECEIVED

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BA						

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
						YES
						NO

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

BCC	NO	Gospodarowicz et al, "Permissive Effect of the Extracellular Matrix on Cell Proliferation <i>in-vitro</i> ", <i>Proc. Natl. Acad. Sci. USA</i> , 77:4094-4098, 1980
BD	NO	Burgess et al, "The Heparin-Binding (Fibroblast) Growth Factor Family of Proteins", <i>Annu. Rev. Biochem.</i> , 58: 575-606, 1989
BE	NO	Folkman et al, "Angiogenic Factors", <i>Science</i> , 231: 442-447, 1987
BF	NO	Vlodavsky et al, "Extracellular Sequestration and Release of Fibroblast Growth Factor: a Regulatory Mechanism?", <i>Trends Biochem. Sci.</i> , 16: 82-84, 1990
BG	NO	Ishai-Michaeli et al, "Heparanase Activity Expressed by Platelets, Neutrophils and Lymphoma Cells Releases Active Fibroblast Growth Factor from Extracellular Matrix", <i>Cell Reg.</i> , 1: 833-842, 1990
BH	NO	Campbell et al, "Heparin Sulphate-Degrading Enzymes Induce Modulation of Smooth Muscle Phenotype", <i>Exp. Cell Res.</i> , 200: 156-167 (1992)
BI	NO	Oosta et al, "Purification and Properties of Human Platelets Heparitinase", <i>J. Biol. Chem.</i> , 257: 11,249 - 11,255, 1982
BJ	NO	Hoogewerf et al, "CXC Chemokines Connective Tissue Activating peptide-III and neutrophil Activating peptide -2 are Heparin/Heparan Sulfate-Degrading Enzymes", <i>J. Biol. Chem.</i> , 270: 3268-3277, 1995
BK	NO	Gordon-Cardo et al, "Expression of Basic Fibroblast Growth Factor in Normal Human Tissue", <i>Lab. Invest.</i> , 63(6): 820-840, 1990
BL	NO	Freeman et al, "Human Platelet Heparanase: Purification, Characterization and Catalytic Activity", <i>Biochem. J.</i> , 330: 1341-1350, 1988
BM	NO	Gosher et al, "Purification and Characterization of Placental Heparanase and its Expression by Cultured Cytotrophoblasts", <i>Mol. Human Reprod.</i> , 2: 679-684, 1996
BN	NO	Nakajima et al, "Immunohistochemical Localization of Heparanase in Mouse and Human Melanomas", <i>Int. J. Cancer</i> , 45: 1088-1095, 1990
BO	NO	Mollinendo et al, "Major Colocalization of the Extracellular-Matrix Degradative Enzymes Heparanase and Gelatinase in Tertiary Granules of Human Neutrophils", <i>Biochem. J.</i> , 327: 917-923, 1997

EXAMINER: Marianne Dibrino

DATE CONSIDERED

7/13/99

AMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation

Form PTO-1449 (Modified)

Atty. Doc. No.  
910/5Application No.  
09/614,739

RECEIVED

INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION  
(USE SEVERAL SHEETS IF NECESSARY)Applicant  
Marianne DIBRINO ARTZI et al

JUL 15 1999

GROUP 1800

Date:  
July 1, 1998

Group Art Unit:

CANCELLLED

SEARCHED

INDEXED

MAILED

TRADEMAKS

DRAWINGS

PAPERS

DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
CA						

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
						YES
						NO
H						

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CM	NO	De Vouge et al, "Immunoselection of GRP94/Er dopplasin From a KNRK Cell-Specific $\lambda$ gt11 Library Using Antibodies Directed Against a Putative <i>H. parainfluenzae</i> Amino-Terminal Peptide", <i>Int. J. Cancer</i> , 56: 286-294, 1994
CN	NO	Graham et al, "Comparison of the Heparanase Enzymes From Mouse Melanoma Cells, Mouse Microphages, and Human Platelets", <i>Biochem. And Mol. Biol. Int.</i> , 39(3): 563-571, 1996
CO	NO	Kosir et al, "Human Prostate Carcinoma Cells Produce Extracellular Heparanase", <i>J. Surg. Res.</i> , 67: 98-105, 1997
CP	NO	Kosir et al, Abstract 3378, <i>Cancer Res.</i> , 37: 495 1996
CQ	NO	Ernst et al, "Enzymatic Degradation of Glycosaminoglycans", <i>Crit. Rev. In Biochem. And Mol. Biol.</i> , 30(5): 387-444 1995
	NO	Gospodarowicz et al, "Stimulation of Corneal Endothelial Cell Proliferation <i>In vitro</i> by Fibroblast and Epidermal Growth Factors", <i>Exp. Eye Res.</i> , 25: 15-89, 1977
	NO	Haimovitz-Friedman et al, "Activation of Platelet Heparinase by Tumor Cell-Derived Factors", <i>Blood</i> , 78: 789-796, 1991
C	NO	Yelton et al, "Monoclonal Antibodies: a Powerful New Tool in Biology and Medicine", <i>Annu. Rev. Biochem.</i> , 50: 657-680, 1981
C	NO	Friedman et al, "Regulated Expression of Homeobox Genes <i>Msx-1</i> and <i>Msx-2</i> in Mouse Mammary Gland Development Suggests a Role in Hormone Action and Epithelial-Stromal Interactions", <i>Devel. Biol.</i> , 177: 347-355, 1996
C	NO	Soule et al, "Isolation and Characterization of a Spontaneously Immortalized Human Breast Epithelial Cell Line, MCF-10 <sup>1</sup> ", <i>Cancer Res.</i> , 50: 6075-6186, 1990
C	NO	Miller et al, "Xenograft Model of Progressive Human Proliferative Breast Disease", <i>J. Nat. Cancer Inst.</i> , 85: 1725-1732, 1993
C	NO	Nakajima et al, "Heparan Sulfate Degradation: Relation to Tumor Invasion and Metastatic Properties of Mouse B16 melanoma Sublines", <i>Science</i> , 220: 611-613, 1983
CR		

EXAMINER Marianne DIBRINO DATE CONSIDERED 7/13/99

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.